THE JOURNAL OF
NEUROLOGY AND PSYCHIATRY
FOUNDED BY S. A. K. WILSON

VOL. 3. [New Series] JULY, 1940 No. 3

TOPOGRAPHIC STUDIES OF DISTURBANCES OF SWEAT SECRETION AFTER COMPLETE LESIONS OF PERIPHERAL NERVES

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(RECEIVED 26TH AUGUST, 1939)

THE colorimetric investigation of sweat secretion has become of increasing interest in recent years, not only in the investigation of physiological problems, but also as a supplement to the existing methods of clinical diagnosis. It enables alterations in function of different parts of the nervous system to be identified both simply and exactly. As it does not depend on the patient's statements it is often superior to subjective methods and to the tedious method of chronaxie. This applies especially in cases in which partial lesions of a plexus are present and in following the successive phases of peripheral nerve regeneration after total blocking, suture, etc.

In previous papers (Guttmann and List, 1928 ; Guttmann, 1931, 1937) I have described numerous examples of the disturbances in sweat secretion which result from complete blocking of peripheral nerves. It has been shown that in general the area of sweat disturbance resembles that of disturbed sensibility and especially of analgesia, but that it has its own characteristic form and extent. Further observations have rendered it desirable to attempt a more precise analysis of the sweat disturbances in the areas of distribution of disrupted peripheral nerves.

In this connection a detailed investigation has been made of the following different zones. (1) *The autonomous zone :* that area, according to Foerster (1929) and others, in which loss of sensation and anhydrosis are complete

* This work was undertaken with the aid of grants from Balliol College, Oxford, and from the Society for the Protection of Science and Learning.

following blocking of its nerve of supply. This area of skin is, therefore, that supplied solely by the blocked nerve. (2) *The mixed or intermediate zone :* that area which is supplied not only by the blocked nerve but also by those adjacent to it, and in which the loss of sensibility is only partial. Head (1908) describes it as a zone of protopathic sensation, Trotter and Davies (1909) as a zone of hypoæsthesia. It appears in the " sweat-picture " in some cases as an area of hypohydrosis ; in others, especially in experiments with pilocarpine, as an area of hyperhydrosis. The extent of the mixed or intermediate zone of a peripheral nerve is actually larger than that found after total interruption. There is an area of supply which can only be demonstrated when the nerve itself is intact and all its adjacent nerves are totally interrupted. Foerster (1929) calls this part of the mixed zone the subsidiary zone. (3) *The maximal zone :* the complete area of distribution, or the sum of zones 1 and 2. The complete area of distribution of a peripheral nerve is only demonstrable when all the nerves supplying adjacent areas have been blocked. Sherrington and Head described the sensibility which persists after this procedure as " residual sensibility." As I was able to find an analogous area for sweating, I will call this the area of residual perspiration. As already mentioned these zones have attracted the attention of physiologists and neurologists in connection with disturbances of sensation following lesions of individual nerve-trunks (Létiévant, 1873 ; Head, 1905, 1908 ; Sherrington, 1892, 1898 ; Trotter and Davies, 1909 ; Foerster, 1929 ; v. Frey, 1894, 1896 ; and others).

The following method is largely topographic-physiological and has a certain significance in the investigation of the action of subcutaneous pilocarpine on sweat secretion in cases of a total interruption of peripheral nerves. This latter point is of physiological interest and has long been open to controversy.

The following investigations were carried out in the first instance by Minor's starch-iodine method, but in recent years exclusively by the chinizarin method.

The sodium salt of chinizarin 2–6–disulphonic acid is the colour indicator. This dye is a derivative of anthraquinone and, like alizarin, purpurin, and anthraruphin, is employed in the dye industry. On account of its affinity for water, chinizarin must be kept absolutely dry by admixture with sodium carbonate before it is applied to the skin. A mixture in the following proportions is the most suitable : sodium salt of chinizarin–2–6–disulphonic acid, 35·0 gm., sodium carbonate (powdered) 30·0 gm., rice starch 60·0 gm. For particular investigations it is possible to change these proportions. It is important that the ingredients should be quite dry, finely powdered, and thoroughly mixed. The resulting powder is of grey or reddish-grey colour. With a pad of cotton-wool the powder is dusted over the area of skin to be investigated, using moderate pressure to ensure that the orifices of all the sweat ducts become filled with powder. If the sweating is to be produced by sympathomimetic sudorific drugs, 5 or 10 grains of aspirin and one or two cups of hot tea are given before the powder is applied. The patient is then placed under the radiant heat cradle for a variable time, from 15 to 45 minutes, depending on the readiness with which sweating is obtained. During this time careful observations are made of the time of onset, distribution, and degree of sweat secretion, not only in the area of supply of the damaged nerve, but also in those of the adjacent nerves and the corresponding parts of the opposite side of the body. Where sweating occurs the skin takes on a dark blue-violet colour, and the openings of the individual sweat ducts appear as minute dark dots. The dry areas remain light in colour. This colour distinction lends itself to

photography. At the end of the sweating test the powder may be removed with warm water and soap, if necessary with the help of some vinegar.

Comparative experiments using the chinizarin method and other colorimetric procedures have been carried out by Böhm (1937), Plügge (1938), and myself (1937). There is general agreement that the chinizarin method is suitable and most simple.

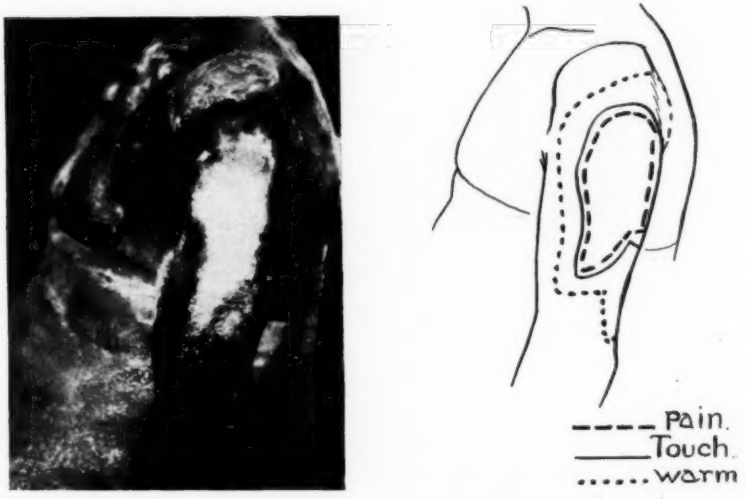
The cause of interruption of peripheral nerves in the cases to be described was traumatic and the classical symptoms of complete loss of motor, sensory, and autonomic functions were present. In numerous cases the total interruption of nerve conduction was verified at operation.

Axillary nerve

Fig. 1*a* shows the result of a sweating-dye-test in a patient with complete interruption of the axillary nerve caused by dislocation and infraction of the head of the humerus. Besides complete absence of sensation in the autonomous zone of the axillary nerve (Fig. 1) a flaccid atrophic paralysis of the deltoid and teres minor muscles was present.

The test was carried out about 4 months after the accident and clearly demonstrated the various degrees of sweat secretion in the area of the distribution of the injured nerve. The anhydrosis in the autonomous zone of the axillary nerve is represented by the white field. The intermediate zone of hypohydrosis is represented in the picture by an area of dark and white spots and patches. The areas of marked sweating in the skin supplied by adjacent nerves appear particularly dark (perilesionary hyperhydrosis).

The variations in the extent and shape of the autonomous and intermediate zones of sweat disturbances following total interruption of the axillary nerve



a *b*

FIG. 1.

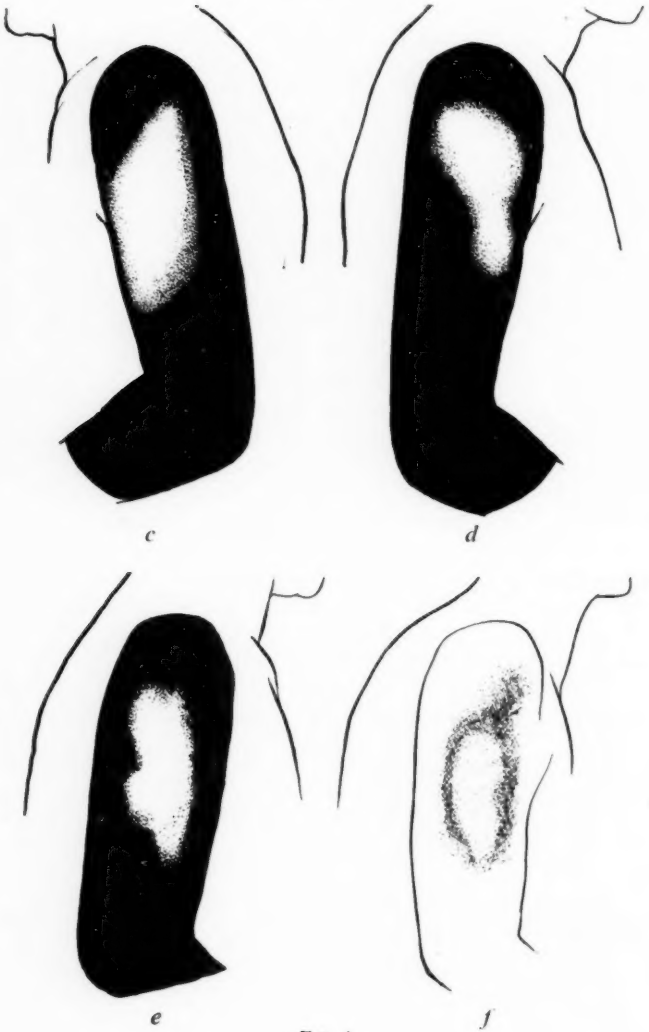


FIG. 1.

are reproduced schematically (Fig. 1*c–e*). These drawings show that the shape and extent of the two zones vary according to the extent of the skin areas innervated by adjacent nerves. Cases 1*c* and *e* had a paralysis of the axillary nerve caused by a fracture of the head of the humerus. There was muscular atrophy with total loss of sensation in the autonomous zone. In Case 1*c* the interruption of the axillary nerve was verified at operation 6 months after the accident. In the case of Fig. 1*d*, there was also an incomplete lesion of the radial nerve with weakness of the extensor muscles of the wrist and fingers and

disturbances of sensation in the distal parts of the area of supply of the radial nerve, caused by a lesion of the right brachial plexus following a motor-car accident.

Following a peripheral nerve lesion the border area of the autonomous zone of a damaged nerve is sometimes revealed, especially in experiments after subcutaneous injection of pilocarpine, by a broad or narrow strip of hyperhydrosis. This is shown in one case (Fig. 1*f*) by the presence of some sweat secretion within the area of supply, indicating that the lesion of the axillary nerve is not complete. Apart from this sweat disturbance this case showed, 5 months after dislocation of the right humerus, an incomplete reaction of degeneration and a diminution of all forms of sensibility in the autonomous zone.

a

b

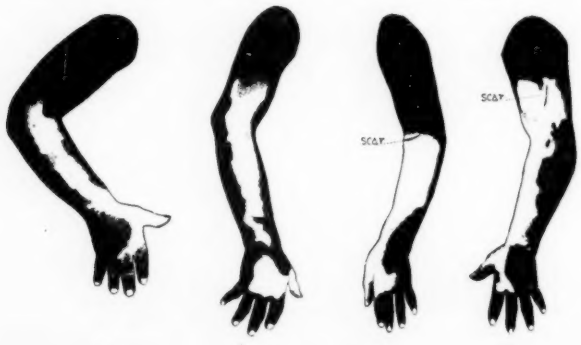
c

FIG. 2.

The maximal zone of the axillary nerve is only demonstrable after interruption of all adjacent nerves, i.e. supraclavicular, radial nerves, medial cutaneous nerve of the arm, and medial cutaneous and lateral cutaneous nerves of the forearm. This is shown in the following case, in which these nerves, with the exception of the supraclavicular nerves, have been interrupted (Figs. 2*a–c*). A young man, aged 18 years, while working at a machine had his right arm caught by a belt and was flung against an iron post, striking it with his right shoulder. Immediately after the accident there was a paralysis of the whole arm. A few days later the function of the deltoid muscle and of the flexors of the right hand and fingers recovered. The paralysis of the flexors and extensors of the forearm and the paralysis of the extensors of the hand, however, persisted and neurological examination 5 months after the accident showed a total interruption of the motor and sensory functions of the radial and musculocutaneous nerves. In addition there was an interruption of the medial cutaneous nerves of the arm and forearm. A complete anhydrosis in the areas supplied by all the completely interrupted nerves was revealed by the sweating test. The maximal zones of the remaining intact nerves, namely, the axillary and ulnar nerves, could therefore be demonstrated. This case shows how far the area of supply of the axillary nerve extends into the anterior and lower parts of the upper arm and how extensive is the area of " residual perspiration " of the axillary nerve. This case also shows the wide extent of the maximal zone of the ulnar nerve on the forearm after interruption of the three cutaneous nerves of the forearm, i.e. radial nerve, musculocutaneous and medial cutaneous nerves of the forearm.

Radial nerve

After complete lesions of the proximal part of the radial nerve, i.e. either above the dorsal cutaneous nerve of the forearm or after interruption of the whole radial trunk above the posterior cutaneous nerve of the upper arm, two types of sweat disturbance may be found. (1) The anhydrosis may comprise one continuous area, as shown in Fig. 3*a*. This occurred in a case of complete



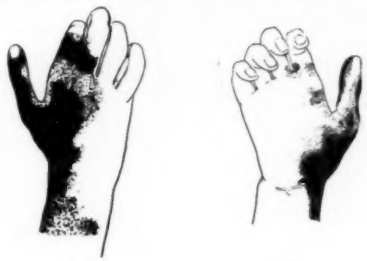
a *b* *c* *d*

FIG. 3.

motor and sensory interruption of the radial nerve above the dorsal cutaneous nerve of the forearm. The neurological examination was made 3 months after fracture of the humerus. Fig. 3*a* shows the continuous area of anhydrosis following the simultaneous interruption of the dorsal cutaneous nerve of the forearm and the dorsal cutaneous nerve of the hand. (2) On the other hand, in some cases of this combined lesion the continuity of the autonomous zone of these two branches of the radial nerve may be absent if there is a larger overlap of the neighbouring nerves. This is shown in Fig. 3*b* on the lower third of the forearm, where the medial and lateral cutaneous nerves of the forearm together with the ulnar nerve extend into the area of supply of these two branches of the radial nerve. In this case the interruption of motor and sensory functions of the radial nerve was caused by fracture of the humerus. The sweating test was made about 5 months after the accident. Likewise after simultaneous interruption of the most proximal branch of the radial nerve, the posterior cutaneous nerve of the upper arm, and of the dorsal cutaneous nerve of the forearm, the continuity of the anhydrotic areas may be absent, due to overlap of the medial and lateral cutaneous nerves of the arm. As the radial nerve supplies a very small area of skin on the upper arm such an interruption of continuity may be frequent in isolated lesions of the radial trunk.

The variations of the overlap by nerves adjoining the radial nerve on the forearm is shown in Figs. 3*a–d*. While Figs. 3*a* and *b* were from cases with isolated paralysis of the radial nerve, Figs. 3*c* and *d* were from cases in which there was also an interruption of the lateral cutaneous nerve of the forearm caused by stab injury (Fig. 3*c*) and gunshot injury (Fig. 3*d*). The two latter cases, therefore, demonstrate the variations of overlap by the ulnar nerve and medial cutaneous nerve of the forearm. In both cases total interruption of continuity of the radial nerve was verified at operation.

The maximal zone of the radial nerve is revealed by residual sweating in its whole area of supply if the adjacent nerves, especially the ulnar and median nerves, are paralysed. Thus, Figs. 4*a* and *b* illustrate the maximal zone of this



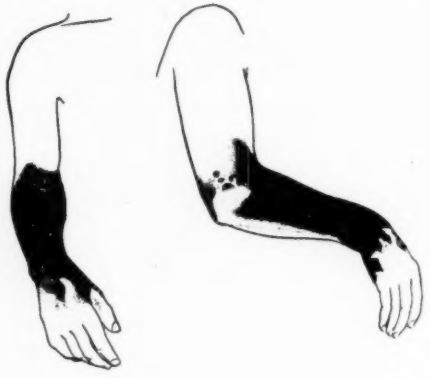
a *b*

FIG. 4.

nerve in a case of total interruption of continuity of the median and ulnar nerves and the medial cutaneous nerve of the forearm, caused by a gunshot wound of the forearm. The lateral cutaneous nerve of the forearm has also been damaged in its lower part. There was paralysis of all muscles of the hand and fingers

supplied by the median and ulnar nerves, with marked atrophy of these muscles, and a contracture of the long flexors of the fingers. In addition, a complete loss of sensation in the area of supply of the severed nerve was found. The sweating test in this case was made eighteen years after the injury. Within the maximal zone of the radial nerve Figs. 4*a* and *b* show the varying degrees of sweat secretion ; the uniformly black area corresponds to the autonomous zone of the radial nerve, and the marginal, patchy and dotted areas of staining indicate the subsidiary or mixed zone which is supplied in conjunction with the ulnar and median nerves. The autonomous zone of the radial nerve on the back of the hand is very small and lies chiefly between the thumb and index finger. The radial nerve also supplies the proximal phalanges of the middle and index fingers (Fig. 4*a*). This area, which shall be considered again in connection with the results of median nerve paralysis, derives a supply both from the radial and the median nerves ; paralysis of one of these nerves in the majority of cases does not abolish sweat secretion in this area. In Fig. 4*b* the subsidiary zone of the radial nerve encroaches considerably upon the area of supply of the median nerve.

The maximal zone of a nerve may also be clearly revealed as a result of an " irritative " lesion of the nerve. Foerster (1929) showed in a study of disturbance of sensibility that the maximal zone of many nerves may extend beyond the areas in which the smallest branches are to be found by dissection. The maximal zone clearly revealed by the sweating test in a case of incomplete lesion of the radial nerve with " irritation " of the dorsal cutaneous nerve of the forearm is shown in Figs. 5*a* and 5*b*. This patient suffered from paralysis and



a *b*

FIG. 5.

partial R.D. of the extensor muscles of his right hand and fingers, relative sensory loss in the area supplied by the dorsal cutaneous nerve of the hand, cutaneous tenderness and intense pain on the dorsal aspect of his right forearm. In addition, he himself noticed that the back of his right forearm was always wet, and the sweating test showed great hyperhydrosis in an area which corresponded

exactly with the area of cutaneous tenderness. This was presumably an irritative lesion of the dorsal cutaneous nerve of the forearm.

Median nerve

The disturbances of sweat secretion on the palm resulting from interruption of the median nerve are illustrated in Fig. 6*a*.

A butcher, using a sharp knife, accidentally cut the median nerve below the wrist. Within a few hours the nerve was sutured. Four weeks later examination revealed a palsy of the two muscles abductor pollicis brevis and opponens and a total loss of sensation in the autonomous zone of the median nerve. The sweating test showed as unstained the extent of the autonomous zone in the palm of the hand, thumb, index, and middle fingers (Fig. 6). The mixed zone of the median nerve was represented by the area of small black dots. This zone illustrates, therefore, the considerable overlap of the radial and ulnar

FIG. 6.

nerves upon the median nerve. Variations in the extent of the autonomous and intermediate zones on the volar surface of the hand following total lesions of the median nerve are shown in Fig. 7*a—f*. Fig. 7*e* shows results of the test in a subject who had a traumatic palsy of the lateral cord of the right brachial plexus with complete interruption of the median nerve. Figs. 7*b*, *c*, *d*, and *f* illustrate results in the presence of lesions of the median nerve above the wrist. Fig. 7*a* is the picture obtained following interruption by gunshot injury of the median nerve in the middle third of the forearm. The complete interruption of the continuity of the nerve was verified at operation.

It is evident that there is considerable variability in the size of the autonomous

and mixed zones of the median nerve. In some cases the autonomous zone may involve the greater part of the palm and the volar surfaces of the fingers with the exception of the little finger. In other cases the autonomous zone may be so small that the mixed zone of the ulnar and radial nerves on the palm may overlap it. The proximal border of the autonomous zone of the median nerve on the palm of the hand may come to a sharp point (Figs. 7*a* and *b*) or, take the form of a more or less blunt arch (Figs. 7*c* and *d*) at the junction of the radial and ulnar boundaries of the area of anhydrosis.

That the sweat glands of the ball of the thumb are supplied less by the median nerve than by the radial nerve has been demonstrated already in Fig. 4*b*.

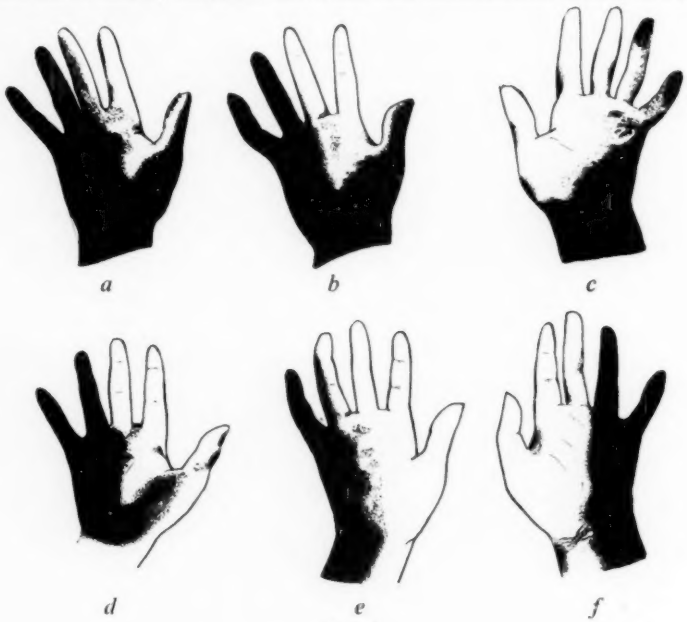


FIG. 7.

The same fact is illustrated in Figs. 7*a* and *b*. Some participation by the radial nerve in the supply of the ball of the thumb is seen in Fig. 7*c*, while there is none in Figs. 7*e* and *f*. An interesting variation (Fig. 7*d*) is an area of very intense sweating on the ulnar side of the ball of the thumb, whilst the radial side of the thumb shows but little sweat secretion. The anatomical basis for this may be the well-known macroscopic anastomosis between the superficial branches of the ulnar and median nerves.

The anhydrosis on the volar side of the fingers following lesions of the median nerve involves the two phalanges of the thumb, the index finger and the median part of the middle finger. The ulnar side of the middle finger, together with the ring and little fingers and the lateral part of the thumb, are involved to a variable extent in the mixed zones of the median and its adjacent nerves.

How largely the median nerve may participate even in the supply of the volar surface of the little finger is shown by the extensive disturbance of sweat secretion following complete lesion of the median nerve (Fig. 7*c*).

Great differences in the extent of the autonomous zone on the back of the fingers are found following total lesions of the median nerve (Fig. 8*a–f*). In all cases the anhydrosis extends on the index finger distally from the middle or distal end of the proximal phalanx, on the middle finger in the majority of cases from the middle of the proximal phalanx. The distal part of the middle finger, especially on the ulnar side, may be within the area of supply of the ulnar nerve and show the presence of sweat secretion (Fig. 8*f*). On the back of the ring finger (Fig. 8*a–f*) anhydrosis and other disturbances of sweat secretion may be nearly absent (Fig. 8*f*).

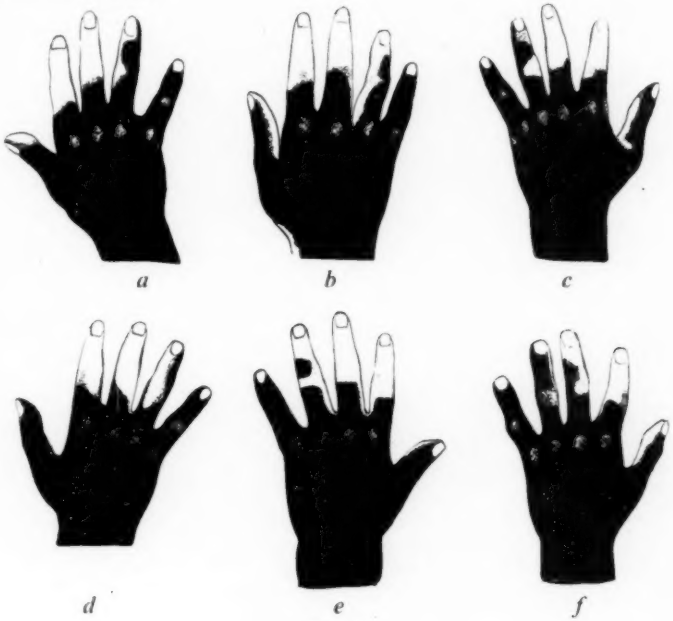
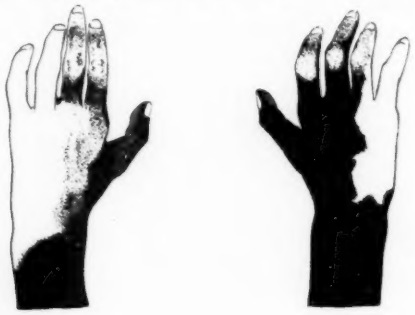


FIG. 8.

Ulnar nerve

In all cases of total interruption of the ulnar nerve the median nerve was simultaneously involved to some extent. It is therefore only possible to consider the relations of the ulnar to the radial nerve on the back of the hand and the fingers. Figs. 9*a* and *b* and Fig. 4*a* illustrate the variations in the extent of the autonomous zone on the back of the little and ring fingers as well as on the back of the hand, which may be found after complete interruption of the ulnar nerve by gunshot injury in the upper third of the forearm. Figs. 4*a* and 9*b* show the mixed zone of the ulnar nerve with the radial nerve, and how extensive this

zone may be. A clear conception of the whole area supplied by the ulnar nerve on the back of the hand may be obtained from a comparison of Figs. 4*a* and 9*a–b* with Figs. 3*a–d*, which demonstrate the maximal zone of the ulnar nerve on the back of the hand after total interruption of the radial nerve. The proximal border of the maximal zone of the ulnar nerve in its whole extent may only be seen when the ulnar nerve and the medial cutaneous nerve of the forearm are severed. Thus, Figs. 2*a* and *c* show that the proximal part of the maximal zone of the ulnar nerve involves most of the ulnar side of the forearm, while its autonomous zone extends only 2–3 cm. above the wrist joint (Figs. 4*a*, 9*a—b*).



a *b*

FIG. 9.

Common peroneal nerve

Figs. 10*a–d* illustrate the disturbances of sweat secretion following complete interruption of the common peroneal nerve. In the cases shown in Figs. 10*a* and *b* there was an isolated lesion of the peroneal nerve. In those shown in Figs. 10*c* and *d* the sciatic nerve was interrupted. The sweat secretion in the areas of supply of the tibial and sural nerves is preserved in Figs. 10*a* and *b*.

a *b* *c* *d*

FIG. 10.

The area of supply of the sural nerve occupies the whole of the lateral part of the foot and extends with a sharp border to the medial side of the third toe. Fig. 10*b* differs from Fig. 10*a* in that there is an additional small area of sweat secretion at the proximal phalanx of the first and second toes. These charts illustrate the results obtained in the case of a young man who sustained a big hæmatoma of his right knee with a total motor and sensory paralysis of the common peroneal nerve (Fig. 10*a*) and in the case of a young flying officer who, on making a parachute landing, sustained in addition to a dislocation of his right knee a complete rupture of the common peroneal nerve, which was observed 16 months after the accident at operation (Fig. 10*b*). The subjects with lesions of the sciatic nerve suffered their injury following an intraneural injection in the one (Fig. 10*c*), and an injury from the tusks of a boar in the other (Fig. 10*d*).

The four cases show the relations of the common peroneal nerve to the adjacent nerves, especially to the saphenous nerve. The " sweat-pictures " illustrate the variability of the extent and shape of the autonomous and mixed zones of the peroneal nerve especially on its medial side where it overlaps the saphenous nerve.

Suprarorbital nerve

That the trigeminal nerve contains secretory fibres in its extracranial branches is now well established. Figs. 11*a–d* show the disturbance of sweat secretion

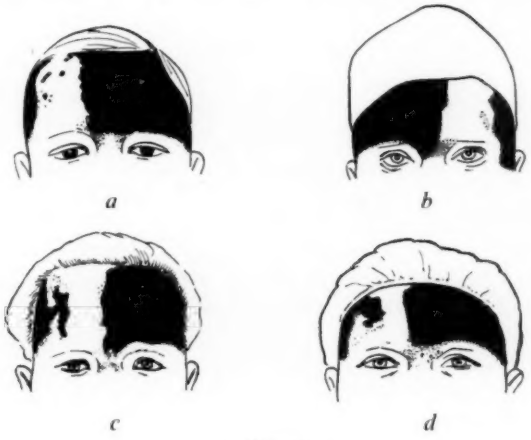


FIG. 11.

in lesions of the supraorbital nerve. After avulsion of this nerve with its frontal branches, performed in four cases, an area of anhydrosis always appeared shortly after operation. This area extended from the superior and medial to the lateral border of the orbit. While the medial border of the anhydrosis up to the edge of the hair line was constant in the majority of cases, there were considerable variations in the lateral border according to the extent of the

mixed zone with the auriculo-temporal nerve on the lateral part of the forehead. Thus in the majority of cases the autonomous zone of the supraorbital nerve only involves a small region above the medial third of the superior orbital border.

Summary

Colorimetric investigation of sweat secretion shows that after total interruption of a peripheral nerve the loss of sweating is complete only within the autonomous zone of the nerve.

The mixed or intermediate zone is revealed by more or less marked hypohydrosis. Following the administration of pilocarpine this zone shows an area of hypohydrosis.

The maximal zone of a peripheral nerve may be demonstrated (*a*) after section of all adjacent nerves (the area of residual sweating) or (*b*) by incomplete lesions of the nerve, characterized by pain and cutaneous tenderness and spontaneous sweating.

In the area of residual sweating the autonomous and mixed zones can be distinguished from each other by differing degrees of sweating.

The demonstration of the different zones in the sweat picture shows that there is great variability in the area of autonomous supply of each peripheral nerve and in the extent of overlap of adjacent peripheral nerves with one another.

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ALZHEIMER'S DISEASE

A REPORT OF SIX CASES

BY

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(RECEIVED 2ND NOVEMBER, 1939.)

THE present paper concerns six examples of Alzheimer's disease met with in a series of 487 consecutive necropsies performed in two mental hospitals, giving an incidence of 1·23 per cent. in those of their population submitted to post-mortem examination. Four of these occurred in a sequence of 48 necropsies, showing the fallacy of estimating frequency on the basis of small numbers. Yet, although the precise incidence of Alzheimer's disease is difficult to assess, it would appear from the experience of several workers that the disease, contrary to what was formerly believed, is not uncommon. For instance, Rothschild and Kasanin (1936) found a 4 per cent. incidence in a series of 234 necropsies performed at the Foxborough State Hospital. The view is further borne out by Mayer-Gross (1938), who reports that seven examples were sent to the Maudsley Hospital for histological examination in 18 months, representing only a fraction of the L.C.C. Mental Hospital material, and also by Newton (1939), who found three instances in a year in a total of about 100 necropsies at Napsbury Hospital where others are under observation in the wards.

In this paper it is proposed, after giving a succinct account of the clinical and pathological findings of these cases, to discuss certain features of their symptomatology and histology, which are of interest in the elucidation of the ætiology of this disease. In the subsequent analysis of the histological factors common to these six cases, particulars will be added of a further instance, described elsewhere (McMenemey, Worster-Drought, Flynd, and Williams, 1939), occurring in a family afflicted with presenile dementia.

In presenting an account of these six cases, it is realized that the anamnesis and examinations, both clinical and histological, were incomplete, yet it is felt that the material is of value in arriving at certain conclusions, the more so, as Jervis (1937) has recently recalled the need for further clinical and pathological reports.

It should be added that in our conception of Alzheimer's disease we are including all those examples of subacute or chronic organic dementia characterized at autopsy by findings of widespread atrophy of the cortical neurones, alterations in the neurofibrils and the presence of plaques, which, by reason of

the subjects' age or on account of severity of pathological lesions, are not suitable for inclusion in the category of senile dementia. After the presentation of these cases an attempt will be made to justify this wider outlook in the definition of Alzheimer's disease and to differentiate this malady from senile dementia.

Case histories and autopsy findings

CASE 1.

A married woman, aged 56 when first admitted to hospital: symptoms consisted of gradually oncoming mental confusion with periods of restlessness which, after a few weeks, necessitated removal to hospital.

On admission, she was confused and unable to give any account of herself. She was of sparse build, emotional, restless, and anxious, sitting up in bed and staring about her in a vacant way, mistaking identities, and pulling continuously at the bedclothes. She was described as " tremulous " with a gait of the senile type, although all reflexes were normal. The heart was enlarged with a systolic bruit at the apex conducted into the axilla; at the aortic base there was a localized systolic bruit and a sharp metallic ring to the second sound.

She became more and more demented, at no time showing any insight into her condition: the loss of memory was great and rational conversation was impossible. Contractures of the hamstrings developed gradually and she became mute, resistive, and helpless. She died in an emaciated state at the age of 62, the illness having lasted 6 years.

Autopsy: The brain was small and weighed 1,012 grammes, all convolutions with the exception of the precentral and postcentral gyri being noticeably smaller and perhaps a little firmer than normal. The atrophy was symmetrically distributed. The leptomeninges were thickened and more opaque than normal, but the Pacchionian bodies were scanty in number. The vessels at the base of the brain were singularly free of arteriosclerosis, in contrast to the findings elsewhere in the body. On cutting the brain, after fixation, the grey matter of the cerebral cortex, and more particularly of the frontal lobes, was noticeably thinned: the ventricular system was slightly dilated. The histological findings were characteristic of an old-standing case of Alzheimer's disease with some thickening of the small vessels. A feature of note was the relative immunity of certain parts of the occipital cortex when adjacent areas appeared to be severely affected; for instance, in some sulci the one convolution was only slightly atrophied and plaques were infrequent, whereas the contiguous gyrus was architecturally disorganized with abundant plaque formation.

The other findings included some coronary atheroma with thickening of the media and proliferation of the intima, and an aneurysmal dilatation of the ascending part of the aorta with scattered plaques of calcification in the arch and descending portion, the disease being active in many parts with some proliferation of the intima and organizing thrombus adherent to it: the elastic laminæ were intact, but there was considerable swelling of the subintimal region with much cholesterol debris and a periadventitial round cell infiltration with commencing fibrosis, without, however, any evidence of mesaortitis. The kidneys were decidedly senile in type, with a thick, fairly adherent capsule, thickened arterioles, a diminution of cortex, and an increase of intramedullary fat. Histologically, there was an early and active interstitial change with very little involvement of the glomeruli and tubules, the capsules were thickened, and there was some proliferation and thickening of the vessels.

Commentary.—The interesting factors are the atherosclerosis of the aorta, coronary arteries, renal arterioles, and, to some extent, of the vessels of the brain. The thickening of the leptomeninges, together with an aneurysmal dilatation of the first part of the aorta, at once suggests the possibility of syphilis, but histological investigations do

not support this view; in fact, the aortitis is characteristically atheromatous, for the media is little altered. The renal changes, however, suggest that widespread functional and organic alterations in the arterioles and precapillaries may be a contributory factor in the pathogenesis of the brain disease, greater than at first appears likely from a histological study of the cortical vessels.

This case, therefore, although clinically typical and histologically characteristic of Alzheimer's disease, is complicated by the presence of a somatic disorder, which, even if not in an organic form, may have preceded the mental illness as a preliminary disturbance of function. As physical signs of the aortitis were present at the first examination, when the mental illness was thought to have lasted only for a few weeks, it is most likely that the generalized arteriopathy antedated the cerebral changes of Alzheimer's disease. A record of the blood pressures would have been instructive. Krapf (1931) has suggested that arterial hypertension, rather than arteriosclerosis, requires consideration in Alzheimer's disease, especially as a factor in the ætiology of epileptiform symptoms.

In this instance the leptomeningeal thickening is greater than in most cases of Alzheimer's disease, but is much less than is usual in neurosyphilis; it is interesting to postulate what would have been the findings had the cerebrospinal fluid been examined on several occasions. An increased cell count would not be unexpected at some stage in the disease. The atrophy of the brain was greater in this case than in any of the series, and this, in itself, might have been sufficient to determine the degree of meningeal thickening. Some degree of atrophy is usual even when, with a short history, the brain weight is not appreciably reduced, as in case VI. Fuller (1911) in a study of senile brains made the observation that 87·5 per cent. of cases with plaques had naked-eye evidence of atrophy.

CASE 2.

A widow, aged 60 when first seen, whose history was not possible because of the absence of relatives, but it was certain that she had been under certificate for 2 years and 7 months in other hospitals. The reception order referred to her as an irresponsible woman who was unable to give any clear account of herself and who presented several delusions, imagining, for instance, that the hospital spoons and forks were her own property.

On admission, the pupils were sluggish in their reactions to light; otherwise, the central nervous system appeared normal. The heart was not enlarged, but there was accentuation of the aortic second sound. There was complete apathy and an absence of emotional response; she was quite out of touch with her environment and the passage of time. On the rare occasions when she would reply to a question it was always with the same answer—" Yes." At times she was very agitated, constantly fumbling with her clothing and wandering aimlessly about the ward. The blood Wassermann reaction was negative.

The dementia became gradually more and more profound, but the agitation persisted. Epileptic fits developed and death occurred at the age of 62 in a stage of emaciation some 6 years after the commencement of the illness.

Autopsy revealed a brain weighing 1,000 grammes, atrophied as a whole, but especially in the frontal lobes, atheroma of aorta, and red hepatization of the right lower lobe of the lung.

Histologically the changes were characteristic of Alzheimer's disease.

Commentary.—The course is similar to the preceding case, occupying 6 years in all, but it was terminated by an acute illness; had the patient survived the pneumonia, the extended lease of life might have led to more extreme changes in the brain.

The patient was one of two of this series who developed epileptiform convulsions. When one considers how universal is the neuronopathy in this disease and how widespread the intercellular alterations which accompany it, it is surprising that the

incidence of epileptiform convulsions is not higher. Although well recognized as a symptom of Alzheimer's disease, convulsions are probably to be attributed to an inherent tendency to epileptic escape phenomena in the presence of brain disease rather than to a specific attack of the pathological process on the cortical cells controlling a particular group of movements. Krapf (1931) maintains that the chronicity and involutional nature of Alzheimer's disease is not likely to give rise to epileptiform attacks without a considerable measure of the epileptic disposition, and that if the underlying diathesis is as strong as this, other precipitating factors met with in the life of the patient will have, in all probability, " brought it out " before the advent of a presenile dementia. Whilst subscribing to the general principle of epileptic diathesis one finds it difficult to accept the contention of Krapf that the pathological process underlying Alzheimer's disease is unlikely *per se* to give rise to epileptiform phenomena without a strong inborn disposition. The decortication can be considerable and the disease is by no means always chronic; in fact, it is often subacute and quite as devastating as general paralysis, so that epileptiform phenomena might be expected in a like proportion of cases were these diseases to be compared in the same age groups. There is, however, a point of pathological importance in this connection: the motor area in Alzheimer's disease enjoys a greater measure of freedom from organic destruction relative to other parts of the cortex, and the Betz cells, in particular, are little damaged. Slight pathological changes were encountered in the Betz cells of both cases showing epilepsy, but similar alterations were also present in others; in case VI, for instance, the changes were not inconsiderable. But it must be emphasized again that histological appearances are no guide in the study of epilepsy, which may be sometimes the result of disturbance of function. The second part of Krapf's contention, namely, that other precipitating factors met with in the life of the patient will have, in all probability, " brought out " the epileptiform phenomena before the advent of a presenile dementia, is offset by the absence, in our experience, of any records of cases giving a previous history of epileptiform attacks, the more so, as the epileptic disposition tends to get less as age advances. It would be interesting to know if the incidence of epileptiform seizures is higher in Alzheimer's disease than in the more chronic and less widespread disorder of senile dementia; we believe this to be the case, although vascular disease, even if unaccompanied by a change in structure, is a likely concomitant over the age of 60, which would tend to make a statistical enquiry both difficult and unreliable. Finally, it must be emphasized that in a greatly demented patient, objective epilepsy only can be recognized: as such patients will, in all probability, be unable to appreciate or describe sensory phenomena, we can have no idea of the true incidence of epilepsy proper in this disease.

The emaciation which characterizes the majority of these cases has several possible explanations, a diminished assimilation of food, either due to anorexia, dementia, or impaired digestion and absorption, to interference with the nutritional centres by the disease, or as part of a generalized disease of metabolism of which the nerve cells are only a part. It is probable that the emaciation is due to many different factors acting at the same time. It may be found in any acute psychosis.

In this connection, however, one recalls the important case of Schob and Guntz (1932); the patient was a woman of 64 who for two and a half years before death had lost weight, becoming progressively weaker and more demented, with loss of hair and teeth. At death her weight was 4 stones 8 lb. The brain, which weighed 960 gm., gave the naked-eye and histological features of Alzheimer's disease, whilst examination of the hypophysis revealed degeneration of the anterior lobe with only a little surviving parenchyma, the rest consisting of connective tissue. The authors describe it as an association of Alzheimer's disease with Simmond's disease, and, while admitting the possibility that the syndrome is coincidental, they suggest that the one disease may cause the other or that both may be attributed to some common factor at present unknown. While it might, perhaps, be said that the evidence for the diagnosis of Simmond's disease, in this case, is inconclusive, especially in view of the known wasting

in Alzheimer's disease, the importance lies rather in the recognition of the possibility of underlying endocrinopathies, especially of the hypophysis, in the presenile dementias. It illustrates the need for a wider approach to the study of these diseases for, from a histological point of view, an examination cannot be regarded as complete which does not include representative sections from the somatic tissues. The possibility of an extracerebral origin for disease of the brain has been emphasized by Globus (1932), MacNamara and Dickson (1932), Ferraro (1933) and by Meyer and Tennent (1936) in Schilder's disease and the same likelihood must be admitted in many other conditions.

CASE 3.

A widow, whose symptoms began insidiously at the age of 57 with mental confusion, loss of memory, and expansive delusions. Dementia followed gradually, certification taking place 3 months later, and death ensued 3½ years after the commencement of the illness at the age of 60 in a state of profound dementia and emaciation (weight 5 stone).

Autopsy showed a brain of 1,180 gm., particularly wasted in the frontal lobes, but also in the superior and, to a lesser extent, the inferior parietal lobules, myocardial degeneration, and patchy consolidation of the lungs, with an area of grey hepatization going on to abscess formation.

The histological features of the brain were consistent with the diagnosis of Alzheimer's disease (Figs. 1 and 2). The general appearance of the frontal cortex, for

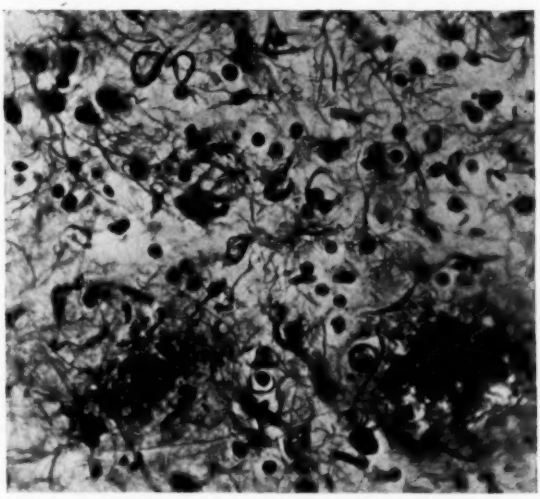

Fig. 1.—Case III: Occipital Cortex. Details can be seen of two plaques and altered neurofibrils in the pyramidal cell layer. (Hortega's double impregnation.)

instance, was one of extreme neuronal atrophy with an abundance of plaques and a reactive gliosis. Neurofibrillary alterations were numerous. In spite of this cortical atrophy, however, there were many areas where the nerve cells appeared quite normal, although a few plaques were scattered amongst them; these minute islets of apparently healthy neurones were scattered irregularly throughout the frontal cortex and their distribution did not appear to be explicable on the basis of a vascular pattern. Oligodendroglia were numerous in the deeper layers of the cortex being aggregated around

nerve cells (satellitosis) and vessels. In the gyrus hippocampus and neighbouring gyri it was noticed that there was much gliosis of the zona molecularis and that many plaques were present in this layer. Altogether, the appearances in this case suggested chronicity, the astrocytes being abundant and hypertrophied around the plaques.

A noteworthy feature was the presence in the cornu Ammonis of granular argentophil deposits of various sizes and shapes in the cytoplasm of the pyramidal cells.

The vessels showed only a minimum of fibrosis.

The general architecture of the cerebellum was well preserved except for the Purkinje cells, which were evidently undergoing a process of degeneration; many cells had, in fact, already disappeared and some showed round them a reaction of small glial cells. The cells of the nucleus dentatus were in a state of commencing atrophy and their fat content was high. There were no plaques in the cerebellum, but some were to be seen

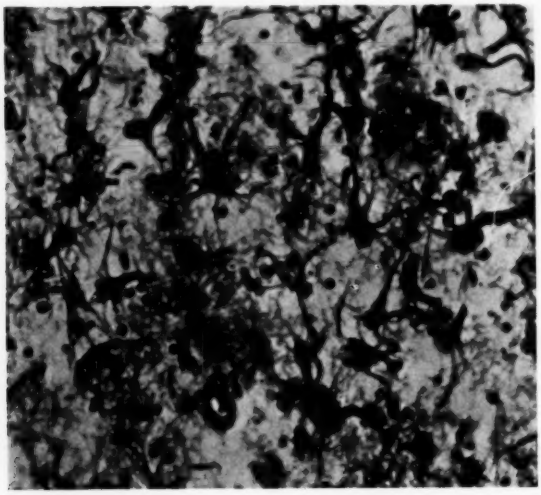

Fig. 2.—Case III: Occipital Cortex. Gliosis of superficial parts. The "cometaria" or comet-shaped glial cells are to be seen especially in the centre of the picture. There are also present plaques and neurofibrillary changes. (Hortega's silver carbonate.)

in the corpus striatum, especially in the putamen, where there was also a moderate degree of nerve-cell atrophy.

Commentary.—The clinical and histological features of the case are characteristic of Alzheimer's disease. Death was attributed to lobar pneumonia.

An interesting feature is the presence of a degeneration in the Purkinje cells of the cerebellum and, also, in the cells of the nucleus dentatus. Simchovicz (1910) recognized and Grünthal (1930) agreed that the Purkinje cells are sometimes diminished in number in senile dementia. Rothschild (1934) describes, in case 1 of his Alzheimer series, great reduction in the number of Purkinje cells with shrinkage of those remaining; the patient, in common with the others, had plaques in the cerebellum, but, in addition, there were a few cerebellar signs. Uyematsu (1923) referred to degenerative changes in the Purkinje cells of some of his senile psychotics as well as the presence of plaques; no relationship was found between them. Critchley (1931) in his Goulstonian lectures recalled the work of Ellis (1918, 1920) on the quantitative reduction of these cells with advancing age. According to this worker the anterior lobe shows the greatest deficiency of Purkinje cells in both subnormal and senescent cerebella.

The argentophil granulations in the pyramidal cells of the cornu ammonis are mentioned by Urechia (1930) as being an infrequent finding in Alzheimer's disease and of a different order from the neurofibrillary alterations; it is presumably the same as the granulovacuolar degeneration of Alzheimer (1911) and Simchovicz (1914).

The vacuolation of the Betz cells would appear to be an unusual finding.

CASE 4.

A married woman, the mother of four children, was admitted to hospital at the age of 59 on account of a sudden nervous breakdown. She was well until 3 weeks before admission when she became confused, depressed, and disorientated. It was thought, however, by her relatives that she "had not been herself" and that her memory had been failing "for some time."

On admission she did not appear older than her years. She was dull, retarded,

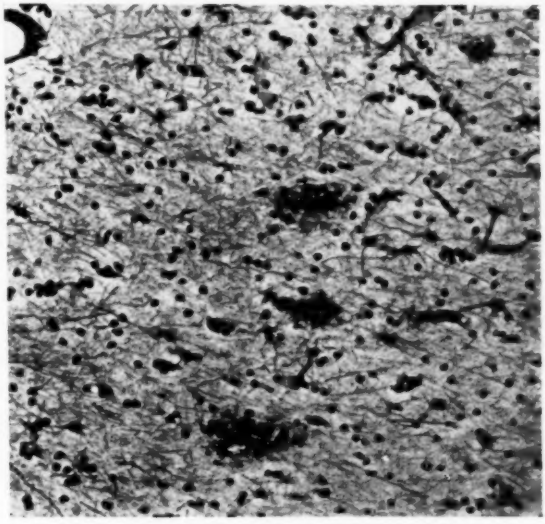

Fig. 3.—Case IV: Occipital Cortex. Plaques can be seen in the white matter limiting the spindle cell layer of the cortex. (Hortega's silver carbonate.)

and, at times, confused and disorientated both in time and place. She could answer only the simplest of questions and that only after much delay. She chattered incessantly, sometimes accusing the nurses of injuring the patients. At times she was restless, wandering aimlessly about throughout the whole day. Her memory for past as well as for recent events was impaired. Her previous and families' histories were negative, as was also the blood Wassermann. The urine contained a trace of albumen, pus cells, and a few hyaline casts.

The dementia progressed rapidly, death taking place about 8 months after the initial breakdown.

Autopsy revealed a brain weighing 1,170 gm. with slight wasting of the frontal lobes, more especially of the anterior ends of the middle and inferior frontal gyri. Different portions of the frontal cortex varied so much in the extent of the disease when examined histologically that it was hard to believe that these samples were from the same case. Nevertheless, the cellular and neurofibrillary alterations were, as a whole, only moderate in severity. Plaques were smaller and more granular than usual,

tending to lack the cellular elements in the centre. The vessels as a whole were healthy, but a few were sclerotic (Fig. 4). Plaques were found in the grey matter which comprised the third nerve nucleus adjoining the aqueduct and ventral and cephalic to the fourth ventricle and also some in the tegmentum. In the cerebellum there was a partial degeneration of the Purkinje cells and also, to a lesser extent, of the molecular layer. The nuclei of the Purkinje cells were pyknotic and many of them gave an irregular contour. There was little in the way of microglial activity and the changes were presumably early.

The other findings included chronic pyelonephritis and brown induration of the myocardium. The kidneys were small and contracted, the capsules being thickened

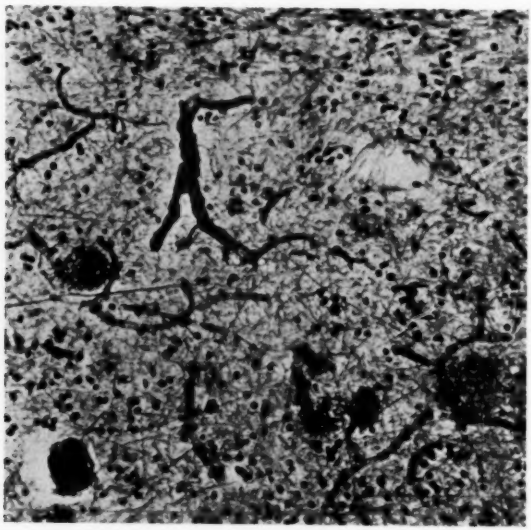

Fig. 4.—Case IV: Occipital Cortex. A sclerotic vessel can be seen in the superficial part: the other vessels are more or less healthy. (Hortega's method of connective tissue.)

and stripping with slight difficulty; the cortex was diminished and the pelvis thickened and chronically inflamed.

Commentary.—The clinical history is that of a rapidly progressing dementia associated with pyelonephritis. Death took place 8 months after the initial breakdown.

Histologically all the features of Alzheimer's disease are present, but the severity is only moderate, as indeed one would expect with so short a history. The changes are most intense in the occipital cortex, and it is interesting to speculate whether or not the disease had been active here for some time before the frontal cortex became involved. It is of interest, too, to note that the postcentral gyrus shows more changes than the precentral convolution. A feature of note is the patchy nature of the changes in the frontal cortex, some areas being destroyed almost completely, whilst the change is early in others. Also noteworthy is the presence of plaques in the corpus striatum and pons, together with the changes in the Purkinje cells suggesting that the disease is widespread.

Plaques have been noted in the white matter by several authors. Fuller (1911) and Uyematso (1923) mention that they occur not only in the subcortical white matter but also in the " very centre of the marrow stalk."

The clinical picture is, therefore, one of acute toxic psychosis and progressive dementia associated with pyelonephritis, and the histological changes show that this psychosis is the result of Alzheimer's disease. Whether the brain changes had antedated the mental illness by long, that is to say, whether in fact the pathological lesions of Alzheimer's disease had for some time been present without symptoms, is speculative, but the possibility cannot be excluded. The renal disease was old-standing, so that it may have induced the specific changes in the brain.

In view of the profound dementia in a person of 59 and the characteristic histology of the brain, even with so short a history, it is difficult to get away from the diagnosis of Alzheimer's disease.

It might of course be said that in this case three points, namely, the late age of onset, the absence of focal signs, the relative paucity of neurofibrillary alterations and the short course, are more reminiscent of senile dementia; but there are certain features which make the alternative diagnosis more likely, namely, the mental illness began acutely, the disease was of short duration and yet alterations were relatively considerable and the symptomatology included the characteristic restlessness and reactive features: the fact that neurofibrillary alterations were not more in evidence is to be attributed to the short course of the illness. Nevertheless, this case does illustrate the frequent difficulty of differential diagnosis, for it lies almost in the no-man's-land between these two diseases.

CASE 5.

A female was admitted to hospital at the age of 58 on account of mental confusion, incoherence, and fits. Little appears to be known of her history previous to admission, except that she was a married woman whose memory had been failing for some time.

She was an undernourished woman showing signs of recent loss of weight. Confused, rambling, and incoherent, she frequently talked to imaginary voices. She could answer only the simplest of questions and she was quite unable to give any account of herself. Her memory was much impaired and she had no trace of insight into her condition. Restlessness and resistiveness were considerable at times. She was faulty in habits. Apart from much dental sepsis there was no evidence of somatic disease. The blood Wassermann and Meinicke reactions were negative. The cerebrospinal fluid was negative in all respects.

During the week following admission she had three major epileptic fits. An exacerbation of the restlessness and mental confusion coincided with a short attack of fever of uncertain nature. The blood pressure during this time was 115/90. Following one of the fits there were choreiform movements of the limbs of both sides. She gradually became more emaciated and demented, taking little notice of questions, but speaking occasionally, towards the end, in a whisper and smiling vaguely when spoken to. Death occurred 5 months after coming under observation.

At autopsy the body weighed only 4 stone 2 lb. There were neither pigmentations nor contractures. The heart was small, the muscle of the left ventricle being firm, indurated, and brown, while the right ventricle was collapsed and the wall swollen and jelly-like. The aorta contained several patches of atheroma, but no calcified areas.

The brain weighed 1,050 gm. and, as a whole, was wasted except for the orbital surface of the frontal lobes and the precentral and postcentral gyri in their upper halves. The atrophy was only moderate in degree and there was no appreciable thickening of the leptomeninges. On section, there was slight internal hydrocephalus. Histologically all the features of Alzheimer's disease were present. The outer part of the sensory cortex showed a fair amount of capillary fibrosis. Here also there were several plaques which appeared to arise in the superficial parts of the white matter, but they were probably associated with the sixth cortical lamina, because they were most frequent in those sections which had been cut rather tangentially. In the cornu Ammonis the glial response was considerable and the impression given was one of

chronicity. Plaques were present, with slight cell atrophy, in the claustrum. There were also plaques in the putamen and a few in the optic thalamus (Fig. 6), but none in the globus pallidus, where, however, there were a few minute calcareous deposits. An advanced alteration in the neurofibrils could be seen in the grey matter adjacent to the median raphe in the pons and there were a few scattered plaques. Sclerosis of the vessels was considerable in some parts, although patchy in distribution. In the medulla the astrocytes showed some clasmatodendrosis in the grey matter and there were a few plaques around the cranial nerve nuclei. With the usual silver impregnation techniques there was a fine granular deposit which appeared to run in palisades both

Fig. 5.—Case V: Cerebellum. Finely fibrillar argentophilic areas are present in the molecular layer; they are mostly acellular and without glial reaction. Some of the Purkinje cells of this case are atrophic. (Hortega's double impregnation.)

traversely and horizontally in the basket cell layer of the cerebellum; under the high power the appearance was finely fibrillary, but under the low power their occurrence in aggregates suggested " young plaques " (Fig. 5). These changes, except in a few instances did not correspond with the vascular pattern. As they were not present in all preparations they were possibly artefacts. The changes in the Purkinje cells and their fibres, consisting of argentophil granulations in the nuclei of the former and irregularity of staining of the latter, could not be regarded as strictly pathological because they might represent only an agonal or even post-mortem change. The cells of the nucleus dentatus were partly atrophic.

Commentary.—Unfortunately the patient was under observation only for 5 months

before death, and it was not possible to say how long she had been ill before certification. It seems unlikely that she could have avoided certification for long with a disease so extensive as this, so the chances are that the clinical course was short, probably not more than 1 year.

On the histological side the findings are characteristic of Alzheimer's disease and again there are plaques in the putamen, as well as in the optic thalamus, pons, and medulla.

A point of interest is the appearance of plaquelike argentophil deposits in the

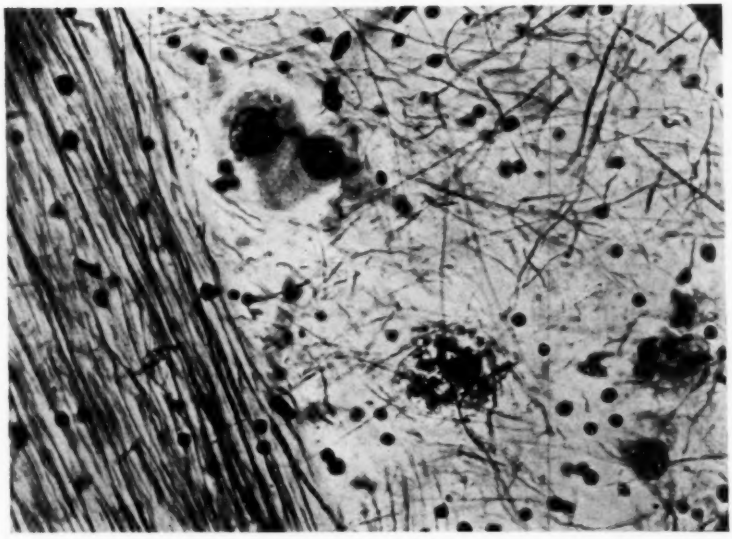

Fig. 6.—Case V: Basal Ganglia. Showing a plaque in the optic thalamus. (Hortega's double impregnation.)

molecular layer of the cerebellum. They are, however, indefinite and in their staining reactions capricious; they are granular and without cellular elements (Marinesco's type I). They are possibly identical with the structures mentioned by Creutzfeldt and Metz (1926) under the name " Filzwerke " in the molecular layer of the cerebellum in a case of Alzheimer's disease and in another case of presenile dementia.

Rothschild (1934) found plaques constantly in the cerebellum in his series of cases of Alzheimer's disease and they have been recorded also by Barrett (1913) and Hannah (1936). Fuller (1911) did not find plaques in the cerebellum of any of his series of 93 elderly brains, neither did Tiffany (1914), but Uyematsu (1923) noted them in a few of his series of 100 senile psychotics, whilst Gellerstedt (1933) found them in two of his series of 50 brains of old age; in one case they were in the molecular layer, in the other in the Purkinje cell layer; they are both illustrated as typical plaques and not resembling those met with in this present case.

The accompanying somatic diseases, which may have played some part in the conduct of the mental disorder, were extreme dental sepsis and a severe degree of degeneration of the myocardium.

CASE 6.

A female was admitted to hospital at the age of 61 on account of excitement and restlessness. She was quite well until 3 months before admission, when, on account of a lifelong history of dyspepsia, which had become worse during the last 3 years, she was persuaded to go into hospital for an operation on her gall bladder. This was undertaken soon after entering hospital and the gall bladder was removed together with stones and the patient made a good recovery, leaving hospital some four weeks later. Her husband noticed a change in her soon after this, for he remarked that she had become quarrelsome and cantankerous, and he attributed these symptoms to her recent operation. Later she became noisy, restless, and confused and it was necessary to send her to hospital. She had three children, all of whom were well.

On admission she was confused and unable to answer questions or give any account of herself, wandering away when spoken to and muttering to herself. Her facies betrayed anxiety and she kept asking if she could " go to the party." She was noisy and destructive and at times resented any attention or interference. Physical examination revealed little apart from signs of myocardial degeneration. The blood Wassermann and Meinicke reactions were negative.

Throughout her stay in hospital the most noticeable features of her illness were the restlessness and confusion. Her appetite was poor and it was with great difficulty that she could be persuaded to take her food. The restlessness became extreme and was accompanied by cough, dyspnœa, and swelling of the ankles, and death occurred suddenly, the mental illness having lasted in all about 8 months.

At autopsy, the heart was small and showed brown induration of the myocardium, the right chambers being a little dilated; the valves were healthy, but the coronary arteries were decidedly thickened, although far from being occluded. The aorta showed only slight patchy atheroma. The liver was chronically congested and fatty, the gall bladder was absent, and in the common bile duct there was the head end of a rubber catheter draining into the duodenum; there were no post-operative adhesions nor signs of inflammation.

The brain weighed 1,300 gm., but in spite of this there was atrophy of the frontal poles and inferior parietal lobules, the leptomeninges being slightly but distinctly thickened. The vessels of the base were free from naked-eye evidence of arteriosclerosis. On section, the lateral ventricles were moderately dilated and the choroid plexuses were cystic. Histologically the findings were those of Alzheimer's disease. The Betz cells had not escaped destruction in this case and there were plaques in this layer. There were plaques, too, in the lamina molecularis, but they were of the " granular " type and not typical. There were a few plaques to be seen in the claustrum, putamen, globus pallidus, and optic thalamus. The changes in the globus pallidus exceeded those in the putamen, the cells being partly atrophic. The astrocytes had undergone a fibrous transformation and many of them had an argentophil material adherent to the processes. There was some calcification of the vessels in the globus pallidus.

Commentary.—The facts of interest in this case are the relatively late onset at 61, the rapid history of only 8 months, characterized by restlessness and confusion ensuing a month after cholecystectomy, and the sudden death. This last feature has been noted by Rothschild (1934), who suggests that it may be due to disease in the basal ganglia or vegetative centres. In the present case plaques were found in the globus pallidus and optic thalamus, as well as in the putamen, and there was, in addition, a sclerosis and calcification of the vessels of the globus pallidus. Rothschild and Kasanin (1936) have commented on the relative invulnerability of the globus pallidus, but Gellerstedt (1933) described plaques in the pallidum of four out of his 50 cases of senile brains.

Other points of interest are the low weight of the patient on admission, 5 stones 11 lb. falling to 4 stones 6 lb. at death, and the findings of coronary artery sclerosis and terminal capillary bronchitis.

Again the histological findings are characteristic of Alzheimer's disease and the clinical symptomatology is atypical only in its short course. One wonders if the foreign body could have, in any way, contributed to or influenced the course of the illness.

Histological analysis of six cases

Some authors have found it convenient to enumerate the senile plaques. Simchovicz (1910), for instance, has elaborated a method of counting so many per field under standard optical conditions. The labour can hardly be justified, however, in view of the fact that so many brains tend to shrink, with resulting condensation of plaques; for not only will the "packing" of the cellular elements depend upon the age of the brain, the pathological process, and its duration, but also upon the mode of death, the agonal fluid changes, delay before and mode of fixation, rate of freezing and alterations caused by impregnating reagents and mounting; moreover, the count depends upon the resultant of these changes as they affect three dimensions.

Partly for these reasons, but more because the distribution of the lesions in these cases was so often patchy, especially in those with the shorter clinical course, it was decided that a less accurate method would suffice. Accordingly, a rough estimate of the changes was made in several areas of cortex and the six cases were compared at the same examination and the results set down alongside each other. This method of assessment is, of course, open to many objections; it is not always possible, for instance, to compare the identical portion of cortex in two brains or even to obtain a section cut absolutely at right angles to the surface; the patchy nature of the changes in some of them makes it difficult to give more than an average for the whole of that particular area of cortex; but, having in mind these shortcomings, the markings given under the headings of cell atrophy, neurofibrillary alterations and atrophy, and plaques represented the impression gained when the six cases were compared side by side.

The following conclusions were drawn:

1. The atrophy may involve most of the neurones of the cortex, and other highly organized cells such as the Purkinje cells may be affected. The Betz cells seem to escape destruction, but are sometimes altered (case VI, for instance).

2. In general, the intensity of the three types of change runs parallel; that is to say, plaques are most abundant where cell atrophy is greatest, and atrophy of the neurofibrils, together with the more spectacular and characteristic " tangles " and " loops," when present, runs parallel with both; there are exceptions to this, as, for instance, in the outer and, to a less extent, the inner granular layers, where sometimes plaques are scanty, although cell atrophy is extreme. Rothschild (1934) commented on the correspondence between the intensity of the three components of the characteristic histology, viz. non-specific cell alteration, plaque formation, and neurofibrillary change. Perusini (1910) and later Grünthal (1930, 1936) remarked on the parallelism between neurofibrillary

alterations and plaques. Barrett (1913) noted a maximum incidence of plaques in the cerebellum in those places where atrophy of the nervous elements of the molecular layer and alteration of Purkinje cells were most marked.

3. The changes are most extreme, as a rule, in the outer three layers. Plaques were numerous and atrophy extensive in the internal granular layer of the sensory cortex of case II. In case IV, however, this layer was well preserved in the occipital cortex whilst the spindle-cell layer contained more plaques than in any of the others examined: moreover, quite a few could be seen in the white matter immediately deep to the cortex (Fig. 3). In this case the second and third layers were also severely affected in the occipital cortex. Plaques were also noted in case III in the white matter deep to the motor cortex.

4. When the frontal and occipital cortices are compared, the changes in the former are slightly in excess of the latter in cases III, VI, and VII, while the reverse holds in cases IV and V. Comparing the six brains together, the frontal and occipital cortices are almost identically afflicted as regards severity of the process. Simchovicz (1924) maintained that plaques were most abundant in the occipital cortex in Alzheimer's disease and in the frontal lobe in senile dementia. Jervis (1937) was unable to confirm this observation, concluding that the differential diagnosis between these diseases was not possible on the basis of the numerical distribution of the plaques. Our experience agrees with the latter author.

5. The most altered part examined is the insula of case V (the history and course of which were short); the next most diseased area is the frontal cortex of case II. In general, however, the most intense changes correspond with the longest clinical course, but there are exceptions. The frontal cortex reveals more extensive lesions in the chronic cases II, III, and VII, than in those with the short histories, i.e. cases IV, V, and VI. Our experience agrees with that of Rothschild (1934), who maintains that there is no direct relationship between the severity of the illness and the number of plaques. On the other hand, it would seem as if the case with a short clinical course is associated with a smaller, more granular, and less cellular plaque than is met with in instances of the disease which have survived many years. Case IV was an example of this.

6. In general, the motor and sensory regions are damaged less than the frontal and occipital cortices; an exception is case VI where the changes in the pre- and postcentral convolutions exceed those in both frontal and occipital areas; it is noteworthy that this case was of short duration only and epileptiform phenomena were not evident.

7. The changes in the gyrus hippocampus are similar in extent to those in the frontal cortex, but, in general, they are not so severe. The distribution of lesions in the cornu ammonis, however, is erratic; most changes are found in case I, whilst there are few only in cases III (chronic) and VI (acute); in two the fascia dentata is extensively affected; in three it is intact.

8. Characteristic lesions in the corpus striatum, especially putamen, are usual, whereas the globus pallidus and optic thalamus are less often affected; Urechia and Danetz (1924) noted that plaques are more frequent in the striatum than in the pallidum. The frequency of changes in the corpus striatum is

worthy of note and it is probably to be accounted for by reason of the known embryological unity of this ganglion with the cerebral cortex (prosencephalon).

9. The choroid plexus does not show changes other than those usual for the âge of the patients. This confirms the observation of Rothschild and Kasanin (1936). It will be recalled that in the juvenile case of Malamud and Lowenberg (1929) the alterations in the choroid plexus were extensive, amounting to degenerative changes in the vessels of the villi. For this reason the choroid plexus deserves careful consideration in any histological study of this disease.

Current theories as to the nature of senile plaques and the significance of the histological changes in Alzheimer's disease

Blocq and Marinesco (1892) are usually credited with having been the first to describe the senile plaques. In the brain of an epileptic they spoke of " petits amas ronds du diamètre de 60μ environ." They called them " plaques sclereuses de nevroglie " and the term " plaques seniles " was first given to them by Simchovicz in 1911, who believed that their absence was against the diagnosis of senile dementia.

The nature of senile plaques has been well dealt with by many authors and it would serve no useful purpose to give more than an outline of the recent theories advanced, both as to their origin and life-history; the subject is rendered difficult to some extent by reason of a confusion of terminology, especially in regard to the essential origin of the plaque. Amongst early papers of importance are those of Redlich (1898), Alzheimer (1907), Fischer (1910), Perusini (1910), and Fuller (1911). The most valuable post-war accounts are given by Uyematsu (1923), Critchley (1929), Ferraro (1931), Braünmuhl (1931, 1932), Marchand (1932), and Bouman (1934). Uyematsu classified plaques into four types: (1) a spheric form with a nuclear-like central mass; (2) a spheric form without a nucleus, found abundantly in severe cases; (3) a perivascular variety; and (4) a diffuse spheric type with a globule-like centre found especially in the region of the large pyramidal cells of Ammon's horn. Marinesco (1928) grouped them into three stages of development: (1) argentophil granular deposits of irregular contours and without cellular components; (2) a plaque through the centre of which pass the swollen processes of microglia; and (3) a type consisting of an argentophil filamentous wreath containing a clear space and in the middle one or many microglial cells with pyknotic nuclei and swollen processes. In referring to the anatomy of the plaque and its essential origin, Uyematsu (1923) says: " The structure common to all (plaques) is the court (Hof) which consists of dark-stained fibrils of indefinite characters. This part represents, in all probability, a destructive process of the ground tissue following the primary thickening of the neuroglial reticulum. The primary thickening of the reticulum is considered to be a reaction to the various degenerative processes of the ectodermal and mesodermal elements such as ganglion cells, neurofibrils, glia cells, glia fibres, blood vessels, and products of pathological metabolism. So far as the nature of the pathological metabolism is concerned the writer has no definite conception, although the ganglion cell origin is suspected. The

abnormal reaction of the reticulum . . . may be attributed to primary exhaustion of nutritive energy or a secondary characteristic caused by specific exogeneous agencies." Creutzfeld and Metz (1926) conclude: " The nerve cells and their branches, the glial cells and their ramifications are embedded in a ground substance (Grundsubstanz) whose nature and structure we do not know exactly. The feltwork (Filzwerk), the network of filaments (Fadchengeflechte), and the plaque nuclei are either particular alterations of the ground substance or pathological storings in them."

The origin of plaques has been variously accredited to disease of the nerve cells, axis cylinders, all types of glial cells and their processes, and even to the deposition of abnormal products of metabolism; there is perhaps something to be said for all of them. Ferraro (1931) concluded a careful analysis of the literature and a personal study with the opinion that plaques could originate from either altered microglia (the commonest) or oligodendroglia and sometimes from nerve cells. He laid emphasis on his impression that the microglia and oligodendroglia seem to possess insufficient vitality to elaborate fat, supporting this contention with the well-known fact that gitter cells are rarely found outside the plaques, suggesting that there is an absence of migration of the fat-laden cells. He postulated a particular type of degeneration for these glial eléments, the nature of which is not yet known, and he maintained that these degenerated cells may constitute a small plaque or the origin of a larger one.

Most authors, however, now believe that the role of the microglia and oligodendroglia is secondary. Perusini (1910), for instance, advocated that the plaques had their origin in a disease of the nervous tissue giving rise to a densification of the glial reticulum in which afterwards pathological products of metabolism became encrusted. The most generally accepted view on the causation of plaques is based upon the studies of Marinesco. In 1911 he wrote " on pourrait admettre que l'élément primordial de la plaque est constitué par des principes chimiques qui se deposent dans différent régions de l'écorse à la suite d'un trouble dans l'equilibre colloidal." This view was endorsed by the same author in 1928. The exegesis of the senile plaque was carried a stage further by von Braünmuhl (1931), who identified its origin with the process of " protoplasmahysteresis " advanced by Růžička (1922, 1924); hysteresis or condensation of living substance being, according to this author, the third biological process, the other two being assimilation and dissimilation. Experiments were made to show that the morphology of plaques (primitive plaques) is in keeping with the growth of a chemical substance rather than a cellular organism. His intention was to find out not so much what plaques are, but what they are not and from what they do not arise! Their origin on the basis of " Fällungsvorganges " is stressed and nervous and glial structures are accredited with no part in their birth. In the following year, von Braünmuhl summarized the existing views concerning the condensation of the glial reticulum, namely that a primary destruction of nervous tissue precedes the densification of the glial reticulum (Simchovicz, 1911) or else that a densification of tissue comes first and is followed by the deposition of plaque substances (this view was held by Bielchowsky in 1911). He concludes that the vast majority are examples of

condensation of ground substance (" Grundgewebsverdichtunges ")—or, in other words, plaques have the appearance of a secondary phenomenon and that the material giving rise to plaques (" Plaque formende Stoff ") was originally contained in colloid solution. Marchand (1932) expresses the origin of the plaques as follows: " . . . elles sont constituées par une alteration très localisée du réseau fibrillaire compris entre les différents éléments cellulaires du cortex."

Rothschild (1934) supports the view that the plaques are formed in the intercellular ground substance, but draws attention to the fact that they are most abundant in areas rich in unmyelinated nerve fibres—as, for example, the third cortical lamina and the outer molecular layer of the gyrus dentatus. With regard to the essential origin of the plaques he adds that as they are secondary manifestations only, they are not necessarily an accurate measure of the severity of the primary colloidal change.

A recent development in the study of the plaques is the attempt made by Jervis and Soltz (1936) and Jervis (1937) to differentiate senile dementia from Alzheimer's disease by the intensity of the microglial reaction. They find that there are two types of reaction: the one in senile dementia where the microglia is healthy, and the other in which the microglia show severe degenerative changes; this latter type they believe to be characteristic of Alzheimer's disease. A few years previously, Verhaart (1929) had commented on the role of the microglia, stating that in old age the plaque runs a more favourable course, the Hortega glia " gaining the victory," whereas in pathological states the microglia show evidence of toxic degeneration, and as early as 1911 Fuller, in a study of 93 elderly brains, had remarked that the glial attempts at elimination of deposited products of pathological metabolism and their replacement did not appear successful. Ferraro (1931) commented on the apparent lack of vitality of the microglia and their inability to continue the work which they have begun, adding that " gitter " cells are rarely found leaving the plaque. Hannah (1936) noted absence of microglial reaction in his case of Alzheimer's disease.

A view on the origin and growth of the plaque which is in keeping with the known phagocytic activity of the microglia is that of Hortega (1939). According to this worker there are three stages in the formation of the plaques. First, there is a focal mortification of the tissue (" tejido "); by this word Hortega implies all the elements of the brain, including cells, nerve, and glial; usually the plaque begins in an area which is composed of nerve and glial fibres and in this early phase it is possible to recognize abnormalities in the cylinder axis, such as thickenings in parts with fusiform nodules every now and then. Next, there is the stage of microglial mobilization; these mesodermal cells, in doing this, are fulfilling their normal function of scavenging; they are attracted chemotactically to the necrobiotic focus as to an area of softening and accumulate around it in the shape of a rosette. At the same time, the centre of the plaque becomes more granular, with filaments radiating from it reminiscent of a spherocrystal. This centre sometimes gives histochemical reactions similar to amyloid (cf. Hechst, 1929). The microglia are admittedly altered as other authors have shown, but this change is physiological and has to do with their phagocytic activities. The typical appearances of the mobilized " microglia "

are a reduction in the number and ramifications of their processes, an increase of their somatic protoplasm with the assumption of a more spherical form (Fig. 7c) and a more amœboid career. They are almost constantly present in this stage and in number they vary from one to twenty; quite often there is one in the centre in the cytoplasm of which fat inclusions are to be seen. This second phase is, therefore, one of microglial intervention and it has been regarded by some workers as a pathological change in the microglia. These phagocytic activities of the microglia are the same in both Alzheimer's disease and senile

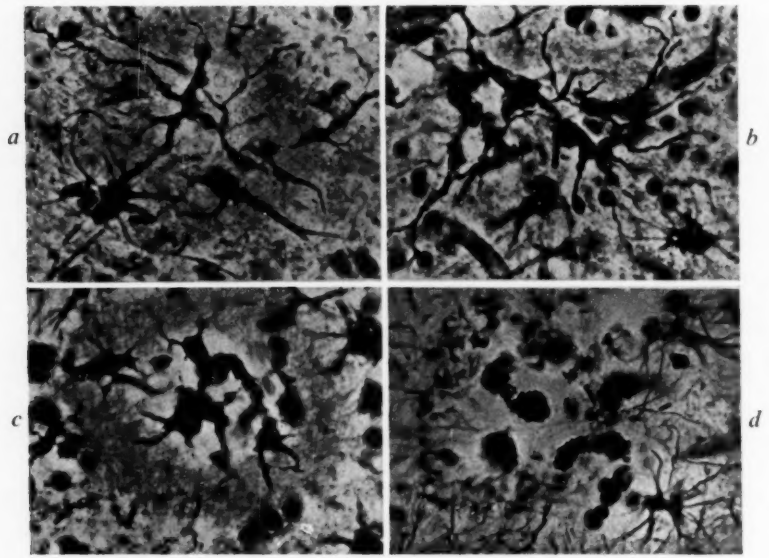

Fig. 7.—Photomicrographs illustrating the varied behaviour of the microglia concerned in the senile plaques:

(*a*) slightly modified forms;
(*b*) cells showing increasing activity;
(*c*) microglia assimilating fat;
(*d*) microglial elements replete with fat and without demonstrable processes (compound granular cells).

(Hortega's method for microglia.)

dementia, the only difference being one of degree; in the former, the disease is more acute and extensive, whereas in the latter the process is gradual and less severe; in the one case the microglia is very active; in the other it is only slightly so. In the third period, there is a characteristic reaction on the part of the astroglia. These cells undergo an alteration consisting of some degree of cellular hypertrophy with fibrous transformation of the protoplasmic fibrils and the apparent formation of new fibres by dissociation of already existing processes. These large glial cells surround the young plaque in the form of a marginal ring, and their fibrous feet penetrate into the centre of the necrotic area in the same way as in a cicatrice. The cells themselves remain at some

distance from the centre of the plaque so that sclerosis of the whole area is seldom compact; the centre, however, is contracted and sometimes a vessel may be detected there. The microglia usually remain in or near the centre of the plaque, (Fig. 7*d*) for it is the exception to see laden phagocytes retiring from the scene of necrobiosis; after many months it is possible that the microglia undergoes a process of degeneration, but there is no evidence in favour of this view. Thus it is that, although nerve and glial processes are usually the first to be involved in a senile plaque, sometimes a vessel is caught up, occasionally a nerve cell, an oligodendrogliocyte, or an astrocyte, and perhaps rarely a microgliocyte.

We believe that this conception of the life-history of the plaque best fits in with our knowledge of the morphological variations found in Alzheimer's disease, senile dementia, and in other conditions.

The origin of the plaque, however, is still a matter for conjecture, although the Růžička-Grünthal hypothesis seems the most likely explanation. The reason for the alteration of the axis cylinders is not known. Bouman (1934) explains these changes, and, indeed, most of the alterations we associate with Alzheimer's disease and senile dementia, on the basis of hyperdifferentiation or " an attempt of the nervous system to differentiate in the direction of a specific neuron, an attempt which may advance beyond the normal." He bases his view on the morphological identity of these changes to those taking place after injury. According to this view, the Alzheimer neurofibrillary changes result when hyperdifferentiation occurs in a ganglion cell, a " torpedo " if in a neurite and a dendritic swelling in a dendrite. If hyperdifferentiation takes place in a neurite which is involved in a plaque there results the eyes, buds, knots, and argentophil fibres, and if it occurs in the nondifferentiated protoplasmic ground reticulum a senile plaque is born.

Apart from the presence of plaques, Alzheimer's disease and, to a less extent, senile dementia, are associated with characteristic changes in the neurofibrils and widespread degeneration of the nerve cells. The first of these changes, which Critchley (1930) regards as constituting the outstanding feature in Alzheimer's disease and which has been explained by Bouman on the same hypothesis of hyperdifferentiation, is associated with the name of Alzheimer (1907), who first described them in his classical case of the disease in a woman of 51 years; he believed that these neurofibrillary alterations in the nerve-cells played a big part in the disease. They consist of an irregular thickening and alteration in the alignment of the nerve fibrils with the formation of loops, tangles, kinks, and often bizarre patterns. The nerve-cell change which is usually associated with the neurofibrillary alteration is readily visible unless the cell has already completely atrophied and disappeared, only the abnormal neurofibrils remaining. If the neurofibrillary alteration is an attempt at hyperdifferentiation, as Bouman (1934) suggests, we must surely imagine that the attempt has failed and the distorted neurofibrils remain as a permanent tombstone to mark the site of the deceased cell. Simchovicz (1910) explained the change in the neurofibrils as a peculiar degeneration attributable to some abnormal product of deposition. Satellitosis and neuronophagia are frequently seen around degenerating nerve

cells, and when the oligodendroglia are for this reason very abundant a characteristic appearance is produced.

Neurofibrillary alterations have been absent in some cases; Fuller and Klopp (1912) could find none in the 300 sections examined from theirs, neither were any present in the second of Lowenberg and Rothschild's (1931) series. It is probably coincidental, but yet worthy of note, that both these examples were associated with toxæmia; the one was of 7 months' duration only in a person with a streptococcal infection of the throat and rheumatism, while the other was the important case with an 8-year remission between the two attacks of toxic psychosis, the first of which developed late in pregnancy, producing a permanent defect. Possibly the absence of neurofibrillary change is attributable to the short course of the illness in these cases, in the same way that their relative infrequency in senile dementia can be put down to the shorter average duration of the illness as compared with the presenile disease. Schnitzler's case (1911) had neurofibrillary changes, but no plaques; this patient is said to have had myxœdema with a gradually oncoming dementia; symptoms began at the age of 31 and death occurred at 36. Urechia (1930) is inclined to regard this case as an example of Pick's disease.

A paper by Alexander (1934) deals with the artificial production of alterations in the neurofibrils. In the absence of other histological features of Alzheimer's disease, neurofibrillary alterations, according to this author, should be interpreted with care. Alexander concludes that in Bielschowsky preparations argentophilia of the nuclei serves as an indicator for the neurofibrillary change produced artificially (by soaking).

Not all neurones, however, which atrophy are associated with neurofibrillary changes. The atrophy of nerve cells, which in this disease may be considerable, is also consequent upon a variety of changes in the morphology of the cell, which are seen to a lesser degree in the brain of many old people; perhaps the commonest of them is a fatty degeneration of the cytoplasm, well exemplified in case III of this series, especially in the frontal cortex. Another variety of alteration is characterized by the presence of argentophil granules of irregular size and shape in the cytoplasm; this was well seen in the cornu Ammonis of case III. This change is the granulovacuolar degeneration of Alzheimer (1911) and Simchovicz (1914). In addition to these findings, shrinkage of the whole cell with pyknosis of the nucleus and an irregular cell outline, pigment deposits in and vacuolation of the cytoplasm, with eccentricity of the nucleus, are common. Sometimes cells are seen which are pale and swollen. None of these changes, some of which may at times be post-mortem in origin, is specific for Alzheimer's disease, and it is not always possible to say how much of the cell atrophy is to be attributed to them and how much is consequent upon degeneration of the neurofibrils; in all probability the latter contributes the most.

The activities of the glia around the plaque and the satellitosis of oligodendroglia have been mentioned already; in addition there is sometimes a tendency for astrocytes to congregate in clusters in the grey matter; we have noticed them not uncommonly in the molecular layer of the cerebral cortex (Chaslin's gliosis,

1891), where the fibrous processes are numerous whilst the cell nuclei are infrequent. The cortical astrocytes nearly all exhibit a fibrous transformation. Clasmatodendrosis was sometimes observed. Curious comet-shaped astrocytes (" cometaria ") were noted, particularly in the occipital cortex of case III (Fig. 2).

In general, the cortical vessels in Alzheimer's disease have been accepted as blameless. Such changes as are present are usually compatible with the age of the patient, if we accept the view that senescence is entitled to a certain amount of vascular change; and if in excess of " normal " it might be said that the alterations are secondary to degenerative changes, the vessels becoming modified by reason of the presence of abnormal products of metabolism. Although the vessels are generally absolved from blame in this disease, a word of caution is necessary in respect of accepting a normal histological picture as evidence of normal function of the tissues; preceding structural alterations in the smaller vessels there are disturbances of function which we are not always able to detect. Marchand (1932) held that the small blood vessels are always diseased in Alzheimer's presenile psychosis. Case I of this series showed more vascular changes than most, but the histology of the great vessels revealed no suggestion of syphilis. The others of this series exhibited only patchy sclerosis of the cortical vessels: in cases II and III it was noted in the frontal cortex, the former giving the appearance of capillary proliferation whilst the latter revealed an aggregation of oligodendroglia around certain of the precapillary vessels. There was sclerosis of the vessels of the occipital cortex in case IV (Fig. 4) and V, of the pons in instances V and VI, and in the globus pallidus of case VI.

Criteria of diagnosis and the relationship of Alzheimer's disease to senile dementia and certain forms of toxic-infective psychosis

Within recent years, in America especially, much attention has been paid to Alzheimer's disease, and valuable papers have appeared which, in addition to presenting further case reports and important deductions on ætiology, serve also to summarize the knowledge available up to date. Amongst the more important of these are the writings of Malamud and Lowenberg (1929), Lowenberg and Rothschild (1931), Rothschild (1934), Rothschild and Kasanin (1936), Jervis and Soltz (1936), Hannah (1936) and Jervis (1937).

The earlier view that Alzheimer's disease amounted only to a senium præcox (Fuller, 1912) was questioned by Barrett (1913) after a study of a case dying at the age of 37. Grünthal (1926) also doubted if the disease could in any way be related to senility. In spite of the present tendency to regard Alzheimer's disease and senile dementia as separate disorders there has been a general disinclination to break away from the custom of associating them as manifestations of the involution of the brain. Rothschild and Kasanin (1936), for instance, believe Alzheimer's disease to be something more than a variant of senile dementia, but the similarity of the lesions suggests to them that like factors may operate, a view in which Jervis and Soltz (1936) concur. Jervis (1937) goes so

far as to assert that in this relationship to senility one may find the only clue in the ætiological interpretation of Alzheimer's disease. These latter authors believe, however, with Grünthal, that histological examination cannot differentiate Alzheimer's disease from senile dementia and they support Kraepelin in the view that the clinical symptomatology is a solid unit and, as such, must play an important role in final diagnosis. They doubt if the disease can be related to senility in view of its known occurrence in the second and third decade. Rothschild (1934) says "the possibility cannot be excluded that Alzheimer's disease may, in most instances, be caused by some underlying factors that lead to senile dementia, but a close relationship between the two is perhaps less frequent than has hitherto been supposed."

Rothschild and Kasanin (1936) describe two cases of rapid clinical course, with a symptomatology of acute toxic psychosis, and, although the histological changes in one of them (case 6) are consistent with the diagnosis of Alzheimer's disease, they are unwilling to accept it as such, because they maintain that to include cases of clear-cut toxic psychosis in the group destroys the concept of Alzheimer's disease as a clinical entity. They remark that Alzheimer's disease is not known in a latent phase and that such an occurrence is improbable in a statistical sense.

That the pathological changes in this disease are not specific is generally agreed. Gellerstedt (1933) in a careful study of the histological changes of the brain in elderly persons found plaques in 84 per cent. of 50 cases when the impregnation method of von Braunmühl was employed. The maximum number was found in the frontal cortex and in three cases the figure exceeded 100 per field. Marinesco (1911), on the other hand, found them only occasionally in his series and Critchley (1931) noted them in only a few of his cases and in two subjects, aged 99 and 102, only a very few were found, particularly in the precential gyri (1929). Apart from "healthy" senescence and senile dementia, plaques have been found, although in small numbers, in some half-dozen different diseases, mostly neurological, and neurofibrillary alterations of the type seen in Alzheimer's disease are known in conditions as far apart as disseminated sclerosis and hibernation in animals. Nevertheless, the presence of *abundant* plaques and neurofibrillary alterations together with extensive atrophy of the neurones is found only in Alzheimer's disease and senile dementia. In the former, the changes are, in the main, both more severe and widespread, although it cannot but be expected that cases dying early in the course of the illness, perhaps by reason of an intercurrent infection, will show fewer of the characteristic lesions. In senile dementia, on the other hand, plaques are usually less plentiful and neurofibrillary alterations are infrequent and may be absent. To this there are, of course, exceptions, and Grünthal (1930) maintains that the alterations in senile dementia are frequently as pronounced as in Alzheimer's disease. The neurofibrillary alterations, for instance, which Critchley (1930) regards as being as characteristic of Alzheimer's disease as plaques are of senile dementia, were found in 85 per cent. of cases of senile dementia by Grünthal (1930) and in 92 per cent. by Rizzo (1924). Both Rothschild (1937) and Lowenberg (1937), however, hold the opinion that senile dementia can occur in

the absence of plaques, although Uyematsu (1923) and Grünthal (1936) maintain that this diagnosis can be ruled out if plaques are wanting.

In general, therefore, it holds that the changes in Alzheimer's disease are of a greater degree of severity than in senile dementia, a view which makes it difficult to believe that the former is only a presenile " senile dementia "; for one would expect a disease associated with, if not attributable to, senility to show its maximum changes in the senior decades and not in the presenium or earlier. On the other hand, if the view that senility is the prime cause of the histological changes be discredited, then the greater amount of tissue damage in Alzheimer's disease can be satisfactorily explained on the assumption that to cause dissolution of a patient with organic dementia requires a greater amount of noxa in the presenile than in the senile age group. To put this in another way, one might say that the young and healthy tissue will tolerate a more severe organic insult than will the tissue whose metabolism is impaired by reason of age. Grünthal (1930), in fact, explained the greater number of plaques in Alzheimer's disease as due to the fact that the process is affecting younger subjects and has, therefore, longer to run. The same argument might, of course, be advanced to account for the essential difference in symptomatology between those diseases so well epitomized by Hannah (1936) who, while recognizing overlapping, described Alzheimer's disease as being characterized by energy misdirected, especially in the early stages, whereas senile dementia is typical of exhaustion of the whole organism from the start; the argument would be that the younger person will resist the oncoming psychosis with a greater reserve of physical and mental energy and will be able to make a determined " attempt at rejuvenescence " (to quote the apt words of Rothschild and Kasanin (1936)), whereas the older person is less able to do so. Stertz (1921) stated this in another way when he talked of senile dementia as part of a general ageing of the constitution, whereas Alzheimer's disease is tantamount to ageing of part of the brain only.

There are other considerations which make it inexpedient to regard the changes in Alzheimer's disease as but a premature senile dementia. The suggestive case described by Malamud and Lowenberg (1929) commencing at the age of 7, after an attack of scarlet fever and proving fatal at the age of 23, is hard to fit into the category of senile disease, especially when there was no suggestion of dissolution of the pars anterior of the hypophysis. Moreover, there are three well-established cases (Perusini, 1910 ; Urechia and Danetz, 1924; and Lowenberg and Waggoner, 1934) commencing under the age of forty, the last of these being hereditary. Two other cases might be added to these, the first, case 7 of Schottky's series (1932), whose symptoms commenced at the age of 41, but with a suspicion that earlier alterations of the whole personality dated from soon after a premature menopause at the age of 37, and the second, a female described by Barrett in 1913, whose illness began at the age of 35, death occurring two years later. The symptomatology of the latter was unusual, but there seems to be no reason for not including it in the category of Alzheimer's disease. Finally, mention should be made of Struwe's case (1929) of a mongoloid woman of 37 with numerous senile plaques in the cortex. These cases all lend support to the view that the disease is not necessarily

associated with an ageing process, although something might be said on the other side for Schottky's case with the premature cessation of menstruation. Lowenberg and Rothschild (1931), on the other hand, report an instance of a woman who gave birth to a healthy child several years after the commencement of the mental illness, a phenomenon incompatible with senility of the somatic organs at any rate.

There is, however, a case to be made out for the abiotrophic view of Alzheimer's disease. It can be said that the histological changes in this malady are of the same order as those of the most characteristic psychosis of old age, namely, senile dementia, and that each represents a pathological parody of those found in extreme old age. The severer changes of the presenile psychosis can be attributed to younger and, therefore, more resistant cerebral tissues, a longer lease of life for the disease, and possibly a more severe form of the disease; moreover, abiotrophy implies a devitalization and premature ageing of the affected tissue, so that senescence of the body as a whole does not have time to take place. A strong point in favour of the abiotrophic view is the occurrence of certain familial examples of Alzheimer's disease.

These conflicting views lead us to agree with the conclusions expressed by Malamud and Lowenberg, and upheld by Jervis and Soltz, namely, that Alzheimer's disease may be caused by a variety of factors. Accepting the Růžička (1922, 1924) conception of " protoplasmahysteresis " as expounded by von Braünmuhl (1931, 1932) it is easy to imagine with Rothschild (1934) that the process as far as the ætiology of the plaques is concerned may be a manifestation of ageing in some instances and of exogenous processes in others. After all, we have in pathology many examples of similar histology being caused by different ætiological factors.

A recent paper by Rothschild (1937) has expressed well the ætiological plurality of the senile plaques. He says " with advancing age, the brain shows an increasing tendency to the formation of plaques, but there may be other factors concerned in their origin and these factors, although still unknown, are largely independent of age and may well differ from case to case. This is in line with the theory that senile plaques may be a manifestation of the ageing process on the one hand, and may represent a general type of tissue reaction on the other." It is not necessary, therefore, to regard Alzheimer's disease as an ageing process; in fact, to approach the ætiology of this disease in an unbiassed way, one should, perhaps, dissociate it in one's mind from senility.

In the same paper by Rothschild there is the important suggestion that the ability of individuals to compensate for brain damage varies considerably and that this difference in reserve power of the brain will account for the fact that some elderly persons afflicted with organic disease of the brain develop senile dementia and others do not. Assuming that this theory is correct and it is in keeping with the recognized views on the importance, in psychiatry, of the pre-psychotic personality, we can understand why some senile dements have fewer organic changes than do persons of the same age who have experienced no disturbance of the mind. A natural development of this theory is to postulate the possibility of latent senile dementia; that is to say, one can imagine that the

senile decorticating process has already begun and the patient awaits only an emotional shock or an attack of influenza to precipitate the onset of symptoms. Depending upon the mental reserve power of the patient the precipitating factor, in order to produce the clinical picture, may need to be considerable or only slight. This view of difference of reserve power in the brain is not confined to the senile age group, for it is well recognized that depending upon the personality make-up and reserve power of the brain, symptoms of dementia syphilitica will be apparent early in some, yet latent and masked in others. Individual differences in susceptibility of the higher cortical centres to the action of excitants and depressants and the rapid deterioration which occurs in a number of general paretics at the outset of malariatherapy are instances of the ready unmasking of latent tendencies.

Similarly, there may exist a " preclinical " stage of Alzheimer's disease, but because of the rapidity of the spread of the pathological process the likelihood of encountering it at its inception is less than in the more leisurely progressing senile dementia. Such potential patients would not be found in mental hospital populations, but elsewhere, and the changes in the brain would indeed be slight in the absence of mental symptoms. Much might be learnt from a study of this disease in its earliest stages; such observations as are available are drawn from biopsies. Flügel (1929), for instance, has reported the characteristic changes of the disease revealed by a biopsy on an early case of organic psychosis; the patient was a 54-year-old man with a 3 weeks' history of dementia. The possibility, therefore, of finding preclinical Alzheimer's disease at autopsy outside a mental hospital is remote. That, as Rothschild and Kasanin (1936) observed, a latent form has not been reported, affords no reason to deny its existence, especially since the total number of cases of Alzheimer's disease reported does not much exceed one hundred.

If, then, one recognizes the possibility of symptoms developing after the commencement of the pathological process then cases previously ascribed to toxic and infective factors such as case 7 of Rothschild and Kasanin's series (1936) might be explained as examples of this process. We would suggest that in deciding whether a case is or is not to be labelled Alzheimer's disease we should be guided by the pathological findings rather than by the clinical history. This is not to belittle the importance of a clinical classification, nor to deny the fact that there is a well-defined symptomatology; neither is it to shut our eyes to the fact that the microscope reveals only a picture of the battlefield when the war is over; but until more is known of this disease, the pathological anatomy is the only rational basis for its definition. In this way, atypical clinical cases, which we believe to be not uncommon, are not likely to be missed. The modern conception of disease has been largely built up on morbid anatomy, and in a subject such as psychiatry, which has apparently little to show in the way of anatomical charges, it is undesirable to neglect any opportunity of correlating morbid symptoms with morbid structures. The clinical conception of general paralysis would not be possible were it not for the histological picture, which has helped in distinguishing its several varieties. The fact, that the ætiology of Alzheimer's disease is not yet determined should not deter us from accepting its

histological picture as evidence of its presence or as forming part of the basis of its classification. The ætiology of many of the diseases of the reticulo-endothelial system is little understood, but this has not prevented the adoption of a classification based on histological rather than clinical features.

There has been a tendency in the literature to regard 2 years' duration as a minimum for the course of this disease, and almost a reluctance to accept anything under this as certain. There is, however, no reason why the course should not be acute; it may, as happened in some of the present series, be cut short by an intercurrent fatal infection before it has had time to advance far enough for the histological features to become marked; or the process may, as we have suggested here, be latent for some time before some precipitating factor serves to make it apparent. Rothschild (1934) speaks of exogenous factors accelerating the progress of the disease in two of his cases; one of them (case III) was clinically at a standstill for 2 years. Case II of Lowenberg and Rothschild (1931) was instructive in that there was a relative remission for 18 years in the course of the illness, during which time a healthy child was born. The two acute phases presented the features of a toxæmia, but the symptoms of restlessness, confusion, and impairment of memory and the findings of abundant plaques serve to establish the diagnosis of Alzheimer's disease. Neurofibrillary alterations were not present. Whatever induced the first attack caused permanent damage, so that it is tempting to think that organic changes were already present after the first attack and that they did not progress materially until the relapse several years later.

The diagnosis of Alzheimer's disease is only certain by biopsy (for which there is sometimes justification) or at necropsy—although clinical and radiological (Guttmann, 1936) evidence can often be convincing. The clinician can differentiate from senile dementia, the separate entities of a widespread (" multifocal ") presenile dementia, and a toxic psychosis of the presenile age group which is associated with dementia; these will constitute the majority of the cases of Alzheimer's disease, but they have to be distinguished from presenile toxic psychosis without dementia and from the host of other dementias, especially arteriopathic, which may occur in the presenium.

We have seen that Alzheimer's disease is not necessarily confined to the presenile age group (40–60). Is it possible, then, to have examples occurring after the sixtieth year? Several authors have published cases over this age which they were convinced were examples of Alzheimer's disease, and they have been criticized on the grounds that the patients were no longer presenile. Hannah (1936), for example, is not in favour of accepting any case after the " middle fifties " as belonging to this disease. Grünthal (1936), on the other hand, gives 50–60 as the usual age of onset, but states that the disease may begin later even until the senium is well advanced. It seems unreasonable, however, to fix a particular age limit for disease, especially in view of the known differences in ageing of families, individuals, and even tissues. We believe, therefore, that each case for consideration as an example of Alzheimer's disease must be judged on its own merits. We have seen that many authors believe that there are differences between this malady and senile dementia, but we must be prepared to

meet with cases on the borderline between the two. Grünthal (1930), for instance, states that alterations in senile dementia may be as advanced as in Alzheimer's disease, and that the only difference is a tendency in the latter malady towards more local symptoms. Until more of these have been described it would seem best to reserve judgment on the question of the upper age limit of Alzheimer's disease.

Our plea, therefore, is to build up our ideas of this disease on the assumption that all cases at any age showing an abundance of senile plaques, neurofibrillary changes, and cell atrophy, which cannot be regarded as senile dementia, belong to the Alzheimer category.

The ætiology of Alzheimer's disease and its classification

After perusal of the literature it is clear that in the past there has been much latitude in defining the clinicopathological entity of Alzheimer's disease and confusion has naturally resulted by reason of the similarity of the organic lesions to those met with in senile dementia. We have suggested the desirability of including in the conception of Alzheimer's disease all examples of subacute or chronic dementia attributable to widespread atrophy of the cortical nerve cells, alterations in the neurofibrils and the presence of numerous plaques, which by reason of their younger age and more severe nature are not suitable for inclusion in the category of senile dementia; we have asked, in other words that, at any rate until more is known about this disease, the histological picture rather than the symptomatology should be the ultimate proof of diagnosis and should serve in arriving at any scheme of classification: in this way we believe that the net will be cast wider so as to include juvenile cases and those examples of subacute toxic psychosis with characteristic histology which are at present tending to be excluded from the confines of this malady.

It is possible to hold the view that the disease is purely constitutional; that is to say that there is some defect in the germ plasm by which ageing processes in the brain may occur before their time (abiotrophy), or one may feel that many extraneous factors can determine a tissue reaction amounting to a series of changes of the kind found in pathological senility along the lines of protoplasmahysteresis. Růžička and Vejnarova (1924), for instance, have shown the importance of inflammatory states in determining protoplasmahysteresis: Malamud and Lowenberg (1929) have published cases of Alzheimer's disease complicated by chronic inflammatory conditions. A case described by Neubürger and von Braunmühl (1930) is of importance in a teleological study of senile plaques in association with dementia; the patient was a man of 56 years who had a traumatic dementia dating back 34 years. At autopsy, numerous senile plaques were found in the cortex with a nerve cell degeneration in the immediate vicinity of the old traumatic focus. It would be interesting to know at what age the plaques appeared.

It seems difficult to get away from the idea that constitutional factors play some part in the ætiology: the occurrence of familial cases of this malady would seem to favour this view; apart from those examples recorded by Schottky

(1932); von Braunmühl (1932), Lowenberg and Waggoner (1934), McMenemey, Worster-Drought, Flynd and Williams (1939), there are possibly others. Rothschild's (1934) case 5, for instance, with a course of 26 years commencing at the age of 44, gave a history suggesting that the patient's mother had had a similar mental illness which also proved fatal. Henderson (1933) believes the process may be dependent on inherited factors. A point of interest is the reference by (Lowenberg (1937) to an example of senile dementia in a father and Alzheimer's disease in the son. There is nothing concrete concerning heredity in senile dementia according to Grünthal (1936), although Meggendorfer and Weinberger are quoted as believing that heredity does play some part.

On the other hand the importance of toxic factors cannot be minimized in certain cases, especially those with a symptomatology of subacute toxic psychosis with dementia.

Boyd (1936) has suggested a subdivision into three groups (*a*) presenile, (*b*) intermediary (hereditary), and (*c*) juvenile. If a classification is sought we prefer emphasis to be laid on the fact whether or not constitutional or exogenous factors are most obvious. For, on the one hand, we have the purely familial examples in which exogenous factors are minimal (Garrod, (1927) says: "in the abiotrophies the tissue defects are the most potent causative factors and the influence of external exciting causes is minimal"), and at the other extreme we have the syndrome of subacute toxic psychosis with dementia and the characteristic histological findings. Between these two we may expect all gradations. The majority of the cases recorded to date appear to lack obvious exogenous factors. It is possible that when the scope of this disease becomes better known more examples of the subacute toxic variety will be brought to light: many present themselves as a confusional psychosis and the dementia is often masked for this reason; moreover, the course of the illness is often short and the brain may be macroscopically normal and therefore not submitted to histological examination. It is quite likely that the disease as we have outlined it will eventually be subdivided into types, for there appear to be at least two clinical varieties.

Summary

Six cases of Alzheimer's disease are recorded with pathological findings.

A plea is made for a wider conception of this disease at any rate until such time as more is known about it, and that this conception should be founded on the pathological histology.

It is suggested that two factors may be involved in any given case; the one endogenous or constitutional and the other exogenous. The former is represented by familial cases; the latter by those examples of subacute toxic-infective psychosis with dementia which present the characteristic histology of Alzheimer's disease. Between these two all gradations may be expected, but most cases and especially the classical type which presents a fairly typical clinical picture, approximate to the endogenous variety.

The importance is stressed for the need for more complete histological

examinations of the other organs of the body. The possibility of extracerebral factor must ever be in mind.

I wish to thank Drs. A. O'Neill and G. H. Shore, medical superintendents of Napsbury and Shenley Hospitals respectively, and their colleagues for access to the clinical records; Professor Hugh Cairns for permission to work in his department; Dr. P. del Rio Hortega for his kindly interest, advice, and help in connection with the technical side of this study, including the photomicrographs; and Sir Farquhar Buzzard for his encouragement.

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BASILAR IMPRESSION OF THE SKULL

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Read at the 25th meeting of the Society of British Neurological Surgeons, Manchester, November 1937.

(RECEIVED 29TH NOVEMBER, 1939)

THE anatomical features of basilar impression of the skull have long been known; its recognition during the lifetime of the patient is extremely difficult on clinical grounds alone, and must be based on accurate radiological examination. In the case to be described in the present paper, planigraphic radiography by the method of Dr. Ziedses Des Plantes (1932) clarified the anatomical details and proved a most reliable aid to diagnosis.

Anatomy and ætiology

In basilar impression the bony margin of the foramen magnum, together with the adjacent parts of the occipital bone, are pressed into the cranial cavity, so that the clivus, which normally takes an almost vertical course from the dorsum sellæ to the anterior margin of the foramen magnum, is elevated to assume a horizontal or even a reversed direction. The angle between the clivus and the planum sphenoidale, varying between 110° to 140° in normal skulls, approaches or exceeds 180°. The vertebral column follows the foramen magnum into the skull so that the axis, remaining in its position between the lateral masses of the atlas, may arrive at, or above, the level of the sella turcica. Abnormal pressure conditions cause skeletal atrophy, and the bony margin of the foramen magnum and the adjacent bone may become paper-thin. The arches of the atlas are subjected to abnormal pressure, and in severe cases even the axis may show pressure atrophy. As a rule the other bones of the skull do not show any abnormalities, but the cervical vertebræ may be malformed or fused.

The first anatomical description appeared at the end of the eighteenth century. A relationship was sought between rickets, cretinism, and basilar impression (Ackermann *et al.*). Rokitansky attributed an ætiological significance to the hydrocephalus present in his cases. Virchow (1877) established the final anatomical picture, based on his own observations and a comprehensive review of the literature, which were extensive even in those days. Virchow excluded rickets, cretinism, hydrocephalus, idiopathic and puerperal osteomalacia (Lucae, 1857; Berg and Retzius), and senile atrophy as causes of

the condition, attributing to them an incidental ætiological significance only. He was impressed by the facts pointing to a geographical distribution of the disorder and stressed the importance of congenital or racial factors. Basilar impression appeared to be more common in Friesland, along the Dutch coast, and in the Bremen district. The frequent co-existence of congenital malformations, particularly those of the hip (Grawitz, 1880), lent support to this view.

In Paget's disease a condition similar to basilar impression may occur. Marie and Léri (1913) described it under the name of "convexobasie," and later Grunthal (1931) and Hanser (1926) reported cases of Paget's disease presenting clinical symptoms identical with those in genuine basilar impression. The two conditions may, however, be distinguished by the appearance of the base of the skull, particularly the margins of the foramen magnum, which are thickened in Paget's disease but atrophic in basilar impression.

Other skeletal abnormalities have been thought to be related with basilar impression. Schüller (1911) mentioned dysostosis cleidocranialis, bathocephaly, in addition to Paget's disease, as favouring its development. He interpreted the X-rays of his own two cases as showing rudimentary formation of the atlas and axis and fusion of the former with the occiput. The relationship between atlanto-occipital fusion and basilar impression was further discussed by Rose and also by Heidsieck. The two conditions frequently coexist, but the atrophic and commonly partial fusions which accompany basilar impression should, with Virchow, be regarded as secondary conditions. They differ from true union of the atlas with the occiput, which, according to Chiarugi (1890) and Bolk (1906) is due to embryological variations in the border between skull and vertebral column.

Attempts have been made by a number of authors to establish a connection between basilar impression and the syndrome of Klippel-Feil. Madame Dejerine * (1926) reporting a case of basilar impression with extensive hydromyelia regarded the condition as congenital, presenting the appearances normally seen in a 40 mm. fœtus. According to the same author, failure of the arches of the cervical vertebræ to close at that stage results in Klippel-Feil's abnormality, and although the cervical arches were completely normal in her own case, she concluded that an intimate embryological relationship existed between the two conditions.

A combination of the syndrome of Klippel-Feil with basilar impression was thought by Merio and Risak to have been present in three personally observed cases. The clinical and radiological features, as reported by the authors, are not at all convincing; the case with the most marked vertebral anomalies had no basilar impression.

Sekir concluded that the two disorders originated from the same developmental defect; from a growth disturbance of the "parachordalia." These are the mesenchymal elements which form the vertebral column and the os tribasilare, and Sekir stressed the important fact that only those bones at the base of the skull which are derived from the parachordalia are affected in

* Mme. Dejerine described this case under the name of "dystrophie osseuse," apparently unaware of the fact that the condition had previously been reported.

basilar impression. Apart from embryological considerations, he based his conception on Mme. Dejerine's hypothesis and on the cases reported by Merio and Risak. Sekir's theory is attractive and more attention will have to be paid in future to abnormalities of the vertebral column in cases of basilar impression.

The fact is that the two conditions have never, so far, been proved to coexist. In basilar impression normally formed bone comes to occupy an abnormal position where it is subjected to atrophic changes; in Klippel-Feil's syndrome the bony defects and fusions, the outstanding features, are primary.

Lordosis of the cervical spine is another vertebral anomaly frequently encountered in basilar impression. Its presence may be revealed by palpation of the pharynx.

The clinical manifestations of basilar impression

A personally observed case may serve as an introduction to the clinical discussion of the disorder.

Mrs. G. R., aged 36. She had been in good health until the age of 19, when for several weeks she suffered from a feverish illness with double vision and slight psychical

Fig. 1.

disturbances. She felt as if she were living in a dream, but was not lethargic. There were neither sensory nor motor disturbances. During the illness she frequently suffered from headache, which in later years troubled her only occasionally. Slight exophthalmos, noticeable in childhood photographs, increased during the illness, and

nystagmus was observed by her relatives. Recovery was slow. Her gait was unsteady when she first got up, and although it improved, it never became quite normal again. Unsteadiness of her hands followed the illness, and still persists. A severe eczema affected her face and neck during her convalescence. Double vision persisted for 2–3 years and then entirely disappeared.

2½ years ago the patient married, and until the birth of a normal child, 8 months before her admission to hospital, her condition remained unchanged. In the last 8 months, however, she became irritable, emotionally hyperexcitable, and often wept without apparent reason. Her memory failed, she was unable to think clearly, and she easily tired both mentally and physically, so that she could no longer do her household duties. She complained of tinnitus in the left ear, but not of deafness. She was seen by a neurologist, who suspected the presence of a posterior fossa tumour, and on the 26th August, 1936, she was admitted to hospital.

Since early childhood, it was learnt later, her head has been implanted on her shoulders in a curious manner. It always remained in a somewhat stiff attitude and the movements of the head and neck were restricted. The illness at the age of 19 did not influence the condition, but some years ago bending the head backwards gave rise to a painful sensation, to a sudden inability to move the head, and to giddiness. These attacks forced her to lie down flat and lasted for about ¼ hour.

Recently the patient had become fatter, particularly around the hips. Menstruation, irregular before her marriage, has been regular since. She did not complain of failing vision or diplopia, was not troubled by nausea or vomiting, and only occasionally suffered from headache.

No other member of the family suffered from a similar condition or from other congenital abnormalities. One nephew is schizophrenic.

Examination.—She is a short squat woman with an overdevelopment of fat around the hips. The mammary glands are within normal limits. The neck is abnormally shaped, the trapezius muscles are large. The neck is so short that the brachycephalic head appears to rest on the shoulders, and hardly one finger can be inserted between the occiput and the vertebra prominens. Neither the occiput nor the vertebral column are tender to pressure. All movements of the head, particularly extension, are restricted by the shortness of the neck, and the head is kept in an attitude of slight flexion. There is a scoliosis of the lumbar spine, convex to the left, and a marked lordosis.

The hands and the right foot are normal, but the second and third toes of the left foot are abnormally long.

Nervous System.—There is optokinetic nystagmus of a moderate degree in both directions, a coarse horizontal nystagmus to the right and left, and a vertical nystagmus on looking upward. Very slight expressional weakness of the right side of the face; the other cranial nerves are normal. The tongue, irregularly shaped and large, shows involuntary movements. On performing Romberg's test she shows a tendency to go to the right. The motor and sensory functions of trunk and limbs are normal. The abdominal reflexes are absent on both sides, and both plantar reflexes are indeterminate, showing an occasional tendency to be extensor. Other reflexes normal. Gait is unsteady, without selective deviation to the right or left. Very slight ataxia and dysdiadochokinesis are the only cerebellar signs.

The respiratory, digestive, and urinary systems are normal. The blood pressure is 170/105, but the heart shows no abnormal features.

The lumbar cerebrospinal fluid pressure is 160 mm. water and rises to 300 mm. on jugular compression. Both rise and fall of the fluid level are slow. The cerebrospinal fluid contains 41 mgrm. per cent. protein, but is otherwise entirely normal. W.R. negative in blood and C.S.F.

Blood count and blood chemistry (calcium, phosphorus, cholesterol) are normal, as is the basal metabolic rate.

Some clinical features peculiar to the present case warrant special comment. Exophthalmos is unusual in basilar impression, and in the present case no cause could be found for it. In two similar cases reported in the literature a colloid goitre (Stenvers, 1928) in one and familial disposition in the other (Biemond), were thought to be the cause of the exophthalmos.

The illness at the age of 19 may have been an atypical encephalitis or the first manifestation of the basilar impression. The latter view is supported by the apparent tendency of the condition to cause clinical signs about puberty and in the presenium (Sinz, Sekir). A new set of symptoms was provoked by the patient's pregnancy; the change in calcium metabolism accompanying pregnancy may have been the exciting factor. Apart from cases of puerperal osteomalcia (Lucae) effects of pregnancy on the course of basilar impression have not been reported.

The fact that the peculiar position of the head was present since childhood argues in favour of a congenital origin of the abnormality; it may be cited against Schüller's assumption that the condition develops within the course of a few years in young persons. If basilar impression is considered to be congenital the gradual or sudden appearance of symptoms in later life must be due to a disturbance of the intracranial equilibrium in the presence of abnormal anatomical conditions. Metabolic and endocrine variations which normally occur during puberty, pregnancy, and the puerperium may, by their effect on the structure of bone, lead to an increase of the basilar impression. Similar observations have been made in Paget's disease, puerperal and idiopathic osteomalacia, and in senile osteoporosis. Infectious diseases may also disturb the cerebrospinal fluid circulation, and although cranial trauma has never been proved to be an important factor, the habitual carrying of heavy loads on the head and neck might provoke a basilar impression in individuals in whom the disease previously existed, as it were, " in anlage."

The cases reported in the literature bear testimony to the difficulties presented by the clinical diagnosis. Boogaard was the first to describe the symptomatology of the condition.* He was followed by Schüller in 1911, who reported two cases, the first to be diagnosed with the aid of X-rays during the patients' lifetime. Schüller classified the signs as due to:

(1) Irritation of cranial nerves in the posterior fossa by traction or pressure.
(2) Blockage of the cerebrospinal fluid circulation.
(3) Pressure on the medulla and cerebellum.

These signs may easily lead the observer to suspect the presence of a posterior fossa tumour, but a variety of other conditions have been wrongly diagnosed in patients suffering from basilar impression. In Stenver's (1928) case hydrocephalic dilatation of the infundibulum had during the patient's lifetime given rise to homonymous hemianopia and dystrophia adiposogenitalis with amenorrhœa, so that the presence of a pituitary adenoma had been suspected. Disturbances of endocrine secretion were also described by Merio and Risak.

* The first of many Dutch papers was by Vrolik.

Astereognosis in both hands, which later became paralysed, was an unusual feature of the case reported by Rose. Glial hyperplasia and cyst formation of the posterior columns was found at necropsy. Mme. Dejerine's patient suffered from tachycardia and rapid respirations in addition to dysphagia and paralysis of the left side of the palate. A psychological disorder may have complicated the clinical picture in this case. Kecht (1932) wrongly diagnosed syphilis in his patient; De Morsier and Junet (1936), Bodechtel and Guizetti (1933) mistook cases of basilar impression for cases of posterior fossa tumours, and in one of his four cases Ebenius (1934) diagnosed a tumour of the quadrigeminal plate.

Radiological diagnosis

The clinical signs presented by basilar impression are by no means characteristic of that condition alone, and even the absence or extreme shortness of the neck is not pathognomic, for it may be found in Klippel-Feil's syndrome and in Pott's disease of the cervical spine. These difficulties may be overcome by the study of accurate X-ray pictures. Unless special attention is paid to the condition of the base of the skull, the abnormality may be overlooked. In two cases reported in the literature (Kecht, Ebenius) scrutiny of the films after necropsy revealed evidence of the disorder which had previously been missed.

In the present case the " impression " was unusually far advanced so that the odontoid process and the lateral masses of the atlas could be clearly seen on the ordinary antero-posterior view. This finding alone established the diagnosis. Should the odontoid process and the atlas be lower, the ordinary lateral skiagrams would not be helpful, for then the atlas and the axis would be concealed by the petrous bones. In these less severe degrees of basilar impression only the sagittal planigram can give a clear anatomical picture of the deformity.

The planigrams of the present case need little comment. The sagittal section shows the upward direction of the clivus, behind it the anterior arch of the atlas and the odontoid process. The posterior arch of the atlas is on a lower level, so that the plane of the atlas is oblique. The occipital squama is also oblique, a feature absent in slight or moderate cases. The obliquity of the atlas allows the deduction that the anterior margin of the foramen magnum must be higher than the posterior.

Vertebral abnormalities can be diagnosed with much more certainty on planigrams than on ordinary films. In the present case the cervical spine was markedly lordotic, but apart from atrophy of the posterior arch of the atlas, which in all probability was fused with the occiput, the structure of the cervical vertebræ was normal. In the lower parts of the vertebral column the 3rd, 4th, and 5th thoracic vertebræ were partly fused and the intervertebral discs in the lower dorsal spine had an oval shape. The lumbar spine was markedly lordotic and scoliotic with a convexity to the left. Abnormal shape of the lower two lumbar vertebræ, the upper part of the sacrum, and both sacro-iliac joints were present.

Fig. 2.—Antero-posterior view of the skull; the arrow indicates the odontoid process.

Fig. 3.—Sagittal planigraphic radiogram (method Dr. Ziedses Des Plantes.)

The fact that the cervical spine was normal excludes the presence of a Klippel-Feil deformity in this case, and the other abnormalities of the spine do not suggest it.

Treatment

Little attention has so far been paid to the treatment of the condition, chiefly because it has rarely been diagnosed before the patient's death. In three cases reported by Ebenius suboccipital decompression was performed. His cases were not far advanced and the operation therefore presented no technical difficulties. It might well be different in severe cases of impression. Apart from technical difficulties and the fact that decompression is only symptomatic treatment, one must consider the possible acceleration of the course of the abnormality after the removal of a large portion of the occipital bone. Under normal conditions the bone which is removed has no supporting function, but in basilar impression the normal planes of support fail and are replaced by

others (Schüller). The posterior arch of the atlas and the posterior margin of the foramen magnum may participate in this function.

A more rational form of treatment was suggested by Sekir, who advocated the use of a supporting apparatus for the head and neck. In the present author's opinion traction on the head by one of the methods in common use ought to prove more efficient. This form of treatment might be followed by the use of a supporting apparatus, once the progress of the disorder has been halted and the patient's condition has been improved. Suboccipital decompression should be reserved for patients who show definite signs of increased intracranial tension.

The patient described in the present paper improved with rest so that no special treatment appeared indicated. She remains under observation and will be re-admitted for more active treatment should her condition deteriorate.

Summary

The anatomy of basilar impression is described. The ætiology of the malformations and its relationship to other skeletal abnormalities is discussed.

One personally observed case is reported, its special features commented on.

The literature on the clinical symptomatology of the condition is summarized.

The value of X-ray diagnosis, particularly planigraphy, is stressed.

The treatment of the condition is discussed.

I am indebted to Dr. Ziedses Des Plantes of Utrecht for the X-rays of the present case. The planigraphic films were taken after his own method.

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Note.—Owing to the war it has not been possible to obtain a complete list of references.

A STUDY ON PURE WORD-DEAFNESS

BY

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(RECEIVED 4TH JANUARY, 1940)

From the Bristol City and County Mental Hospital

ONE of the speech disorders which in the past was studied with great interest is the so-called pure word-deafness. In recent years, however, it appears to have been somewhat neglected, perhaps because the condition is rare and does not appear to fit in well with the modern conceptions of aphasia (Jackson, Marie, Head, Goldstein). Pure word-deafness was described and defined for the first time by Lichtheim (1885) as a speech disorder in which the ability to understand spoken language, to repeat spoken words, and to write from dictation were lost, and, at the same time, the ability to speak, write, and read spontaneously was preserved. In the picture of pure word-deafness there were no paraphasias and the inner speech remained undisturbed. A lack of attention to acoustic sensations was regarded as typical. Lichtheim's observations were confirmed by Wernicke (1874), Wyllie (1894), Ballet (1901) *et al.*, Arnaud (1887), who named the disorder " surdite verbale brute," pointed out that it was characterized by an impairment of the gross hearing of words. According to him the actual understanding of the sounds of words was disturbed, a fact confirmed by other observers. In some of the cases described pure word-deafness seemed to develop from a typical auditory aphasia. In these cases the purity of the picture was impaired by the existence of paraphasias and other signs of disturbance of the inner language. The question whether defects of hearing as well, caused by disturbance of the inner ear could give rise to the condition was discussed by some authors, who expressed the view that labyrinthine lesions might sometimes cause the symptoms of pure word-deafness. This view, however, was questioned when, in a case where an existing bilateral lesion of the labyrinths had been regarded as the cause of pure word-deafness (Freund, 1903), the post-mortem examination revealed a tumour involving the first temporal convolution of the left hemisphere. As the ordinary technique for the investigation of the hearing capacity cannot be employed in pure word-deafness, the use of the Bezold-Edelmann's continuous series of tuning forks was recommended, and it was pointed out that at least that portion of the tone scale known as speech sext (Bezold, 1903), with a proportion of tones for a considerable distance above and below, must be intact before the diagnosis of pure word-deafness could be justifiably made (Bonvicini, 1905). Although we do not propose to quote in detail the bulk of the literature on this subject, we

can assert that, as Weisenburg and MacBride (1935) pointed out, in all cases reported, the purity of the word-deafness was impaired either by disturbance of the hearing capacity or of the inner language.

As to the position of pure word-deafness in the general scheme of aphasia, it is noteworthy that even Lichtheim admitted that preservation of the inner language was an objection to regarding pure word-deafness as an aphasia proper. Nevertheless, he found it necessary to define it as an aphasia as it had so many features in common with the aphasic speech disorders. This view was favoured by the observation mentioned before that pure word-deafness may appear in the course of recovery from typical auditory aphasia. Goldstein (1927) considers that the essence of pure word-deafness lies in the incapacity to comprehend the tones as characteristic speech sounds, although these tones have been perceived. He compares the patient suffering from pure word-deafness to an individual who is in a country where the language is entirely unknown to him. Such a person would not only fail to understand the meaning of the words he hears, but would be unable even to appreciate the combination of sounds as words or sentences. Some workers refused to recognize pure word-deafness as an aphasia at all. Pierre Marie (1906) asserted that he had never seen a case. Van Woerkom (1925) and Mourgue (1920) regarded this symptom as a theoretical construction, and in Head's (1926) scheme of speech disorders there is no space for pure word-deafness.

We have been fortunate enough to encounter and study a case in which the characteristic picture of pure word-deafness was present and was associated with another symptom of additional interest.

Henry G., aged 34, general labourer, was admitted to the Bristol Mental Hospital on 10th April, 1939. On 11th February, 1939, he had been admitted to the Bristol General Hospital in a state of unconsciousness, following a fall from a 'bus. After three days he became clearer and he then gave the impression of being totally deaf. However, from his own statements, made as soon as he had become quite clear in mind, it was evident that his deafness was not of an ordinary character. Otological investigation, to which we will refer later, revealed that there was no gross inability to hear sounds.

After the acute effects of the accident had subsided, the patient was admitted as a voluntary patient to the mental hospital. He described the defect of hearing as an inability to understand spoken words, but, at the same time, insisted that he could hear sounds and noises as well as before the accident. This description of his disability has not changed materially from the beginning. At this point the only reference we will make to his physical state is that of the otological examination. This was conducted by Mr. A. T. M. Wright. The audiometer was employed, as the ordinary methods for testing hearing could not be used in this particular case. The audiogram (air conduction) which we reproduce shows, for the left ear a slight amount of hearing loss in the upper frequencies, and practically normal hearing throughout the scale for the right ear. If the tracings for each ear are compared with the typical tracings of a deaf person, one sees that the impairment of the hearing in our patient was practically negligible. On the average, patients with such an amount of hearing loss show hardly any practical difficulty in normal hearing.

The prominent feature of the patient's disability was the fact that he could not understand spoken language. Investigations into his speech showed the following:

Articulated Speech.—He talked fluently, and without conversational mistakes of a pathological nature. There were no paraphasias and no errors of grammar beyond

what is common for his particular dialect and standard of education. He was, however, noticeably loquacious, especially during the first three months after the accident. His wife confirmed this impression and said that he was much more talkative than he had ever been before. In this way his condition reminded one of the logorrhœa seen in auditory aphasia. This feature tended to diminish as time went on. He had no difficulty in finding words without circumlocution and in forming sentences. There was no dysarthria.

Reading.—He could read correctly and showed that he could understand what he read to himself. He obeyed written orders without errors, even if complicated, such as Head's hand-eye-ear test and other more difficult commands. His response to the commands was equally correct whether he read aloud or to himself. If a number of

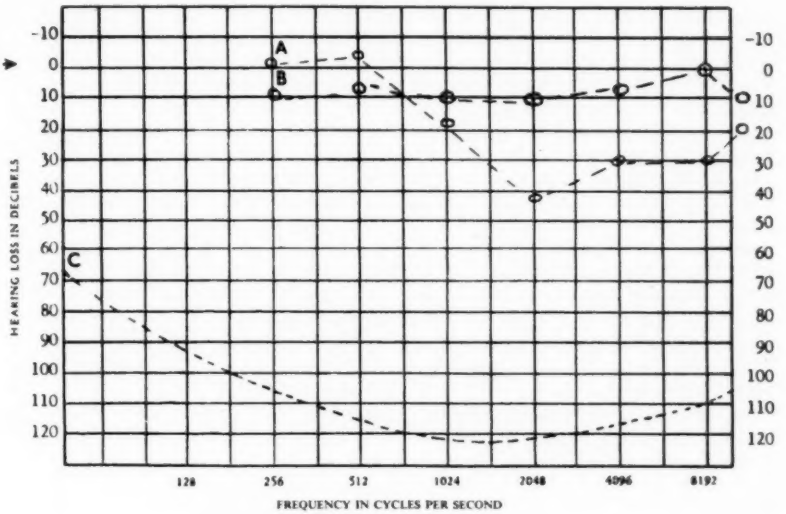

Fig. 1.—Audiometer tracing.

The B dotted line is the record of the right, the A of the left ear. The C dotted line represents the tracing of a deaf person with total loss of serviceable hearing. O: Average normal hearing.

objects were placed on the table and he were requested, in writing, to name any of them, he did so without error.

Writing.—He could write correctly and his spelling was good. His writing contained no more grammatical errors than one could expect from one of his education, and he could write a précis of what he read in print.

Other Intellectual Functions.—He could count correctly and could do simple arithmetic. His drawings were poor, but did not suggest any special disability in this respect. Plan drawing was correctly performed and his orientation in his surroundings was not disturbed. There was no autotopagnosia.

As stated before, the disturbance of speech was confined to the understanding of spoken words. We propose to illustrate this kind of disorder and the patient's attitude towards it by reporting a number of interviews we have had with the patient. These results will be presented as if the interviews were continuous and took place on one day. It seems that, by so doing, a more comprehensive picture may be obtained. Naturally the patient tended to become tired and could not be examined satisfactorily for a long period at one time.

(What is your name?) " Voice comes but no words. I can hear, sound comes, but words don't separate." — (How are you?) " That is letters what you are saying." — (Show your tongue.) " I can't get it. I can hear your voice coming, but it does not finish. Your voice is dead plain." — (Do you feel better?) " Feeling better? I think so." — (How long have you been here?) " Can't get it." — (Close your eyes.) " Can't get it." — (Are you a burglar?) " Can't get it." — (There will be no war.) " That did not separate at all." — (God save the King.) " I can hear you say something." He recognized the melody of the national anthem immediately. The patient added: "There is no trouble at all with the sounds. The sounds come." — (Have you a family?) " Have you something—I could not get the rest." — (Have you children?) " It does not come. The words split up, it does not finish." — (What time is it now?) " What time is it now, did you say? " — (Proverb: early to bed, etc.) " Something about only to-day and something about to-morrow." — (Have you slept well?) " There was four words there. I can hear, but I cannot understand it."

The patient stressed spontaneously that he did not try to lip-read. He added: " I wanted to hear from there. (Pointing to his ears.) I don't want to watch your mouth."

He could imitate melodies without words, provided they did not contain very high tones. He showed a good sense of rhythm. He rarely made a mistake in repeating common sequences, as the alphabet or the early integers. If questioned about his address or his children or asked to repeat very familiar words, he frequently answered correctly. In fact, his understanding for things close to his heart and interests was better than for those of a general nature.

Although he occasionally appeared to understand better when the voice was raised, as a rule there seemed to be no relation between the loudness of speech and his ability to interpret it. The impression, occasionally received, that he was deaf was usually contradicted later in the examination, when the patient might understand quite readily some words spoken softly which he had previously ignored. Sometimes, if one spoke slowly and separated every syllable, articulating clearly, he seemed to understand more clearly, but generally even monosyllabic and short words could not be understood at all. It made no difference to his understanding if the sentences were sung in a well-known melody.

Single letters were not always understood well, as follows: (A) " A." — (I " U." — (O) " U." — (O) " Oh." — (X) " U." — (Y) a sound very similar to U, but with a coughing intonance. — (M) coughing sound. — (I) " Hm ": hum of assent.

Syllables and short words: (Au) " We." — (Au) " Hop." — (H) " Hu." — (If) " Bum." — (And) " And." — (See) " Tea." — (Cup) " Cup." — (House) " If." — (Buttercup) " That is a longish word." — (Schoolboy) " Teatime." — (Schoolboy) " Feeding, did you say? " — (Schoolboy) " That sounded like tea something." — (Match) " All that came was mwoe." — (Town) " Raw, row." — (Bristol) " That's going misda." — (Debt, debt, debt) " That sounds like if, if, if."

When he learned from written information what was really said he was very surprised. When asked if and how he heard the words he spoke himself, he replied: " When I say book, I hear book. Every word I am saying is separate." At another time, however, he indicated that he heard his own words in a similar way to those of other people. (It is obviously impossible to expect the patient to give a clear answer to the question of whether he hears his own spoken words in the form of normal speech or not, as he is quite aware that what he says is correct and he anticipates in his mind from past experience the sounds of the words, with which he has been familiar since he learned to speak.)

It often happened that at a later time in the examination the patient produced some word he had failed to repeat previously. Probably it was by the same process that at times he could eventually repeat a word that had been repeated to him without success several times. He often produced a word which seemed to be the result of a contamination of the word just heard with another, heard some time ago, e.g. (Ashtray)

" Can't get it." — (Medicine bottle) " Matches bottle." — (Matches) " Ashtray." — (Rubber) " Rubber " — (Rubber) " Something there with a ru." — (Rule) " Rule, that's what it sounds like." — (Rubber) " It sounds more like ruler." — (The large key) " Did you say ashtray? "

Very much better results were obtained if the patient had a knowledge of the possible alternatives to the questions and if the number of the alternatives was limited. This was shown by the following experiments: A number of different objects were laid out on the table in front of the patient. He was requested to pick up whatever object was named. This was the result of one such test: (Take the key) key taken. — (Cigarette) " I am not sure." — (Cigarette case) cigarette taken. — (Matchbox) watch taken. — (Inkpot) " It comes in two syllables." — (Handkerchief) no response. — (Where is the ashtray) " I don't get it. I hear it, but it breaks up." — (Take the matches) " That was altogether foggy, that came all on top." — (Penny) penny taken.

Another experiment, similar to that above, was performed. In this the patient was presented with a list of names written on paper. He was then asked to repeat words taken from the list at random by the examiner. (Devon) " Devon." — (Lincoln) " Leicester." — (Gloucester) " None of them. I heard dista." — (London) " Clevedon." — (Salisbury) " I heard lafte." — (Leicester) " Sounded like Bristol." — (London) " Diwan, Devon? " — (Leeds) " Leeds." — (Birmingham) " That sounds like Leeds." — (Oxford) " Lincoln." — (Lincoln) " Lincoln." — (Warwick) " Birmingham, did you say? I heard Bram." — (Salisbury) " It comes like bobo." — (Bristol) " Bristol." — (Bristol) " Leicester." — (Bristol) " Lincoln." — (Oxford) " Could not get it. It appears with a B in front." This examination showed that the same word could produce very different sensations in the patient on different occasions.

Usually the patient appeared to understand conversation better when it concerned his normal sphere of life. Accordingly he appeared to understand his wife and friends more easily than strangers. The following is a specimen of a conversation overheard while his wife was visiting him at the hospital: (Do you want anything brought in to-morrow?) " No, I don't want anything brought to-morrow." — (I might go out on Monday and might take the children on the downs.) " I did not get that." — (I have dug up all the garden) " You have dug up all the garden." — (I left Sam out on Redcliff Hill) " I did not get that." Sometimes the patient did not catch the full meaning of all the words, even if his answers seemed to suggest that he did, e.g. (Do you want a pair of socks brought in to-morrow?) " No. I want only cigarettes." — (What did I say?) " Do you want something brought in to-morrow, but I could not get what."

Very often the patient showed the peculiarity of repeating questions before answering, reminiscent of echolalia, e.g. (How long have you been here?) " How long have I been here? Since yesterday." — (Where did you go to school?) " Where did I go to school? In Bristol." — (How did you sleep last night?) " Did I sleep? Not as well as before."

The patient often complained that what he heard sounded like a foreign language, unknown to him. Summarizing his descriptions of speech as he heard it during repeated examinations and during his daily experience, we found the following to be characteristic and often repeated. " I cannot get it. It does not finish. It's one on top of the other. The words split themselves up. I hear what you are saying, but the pronunciation does not finish. The voices seem to be as clear as it should be. I can hear you quite plainly, but all come on top. I can hear you dead plain, but I cannot get what you say. The noises are not quite natural. I hear your voice, but not the words. I can hear but not understand. It does not pronounce itself."

In contradiction to what has been described by some authors we noticed no lack of attention during conversation, rather the reverse. The patient was always ready to try to understand and to notice changes in tone or rhythm or technique. However, it is certain that his reaction to unexpected sounds, which would have attracted the

attention of normal people, was either lacking or inadequate. He did not turn in response to a shout or clapping of hands or a commotion in the ward, although he was aware that these sounds had been caused. This is borne out by the fact that he could recognize members of the nursing staff by their footsteps. The great importance of this particular defect is demonstrated by the following occurrence. The patient was observed proceeding one morning along the main road of the hospital. He made no effort to get out of the way of a lorry behind him in spite of the loud warning of the horn. That he heard the horn and recognized its character is certain, for he admitted as much with considerable heat when he was forbidden, for his own safety, to walk alone on the main road. It was obvious from his action at the time that when he heard the motor horn he did not react as if it were a sound of warning. This behaviour is of interest in connection with a further symptom.

This special symptom was observed from the beginning and was present at every subsequent examination; that was an alteration of the normal reaction to painful stimuli. Thorough and repeated examination of superficial as well as deep sensibility revealed none of the usual forms of disturbance. What was abnormal was the lack of the normal reaction to pain. When the patient was suddenly pricked, even very strongly, he failed to withdraw the part injured. There appeared to be a lack of the normal reaction of defence and flight from danger. He admitted that he could feel the painful stimulus for what it was. This abnormal reaction was the same irrespective of where the stimulus was applied. One felt at first that he was inattentive to painful stimuli, but in the course of the examination it became obvious that there was no real lack of attention. During the examination the patient never failed to report on every single sensation and to describe correctly whether it was painful or whether it was innocuous. The absence of any defence or withdrawal reaction was clearly shown when a strong, painful sensation was applied by surprise, e.g. when the examiner, standing behind the patient, suddenly pricked his hand or neck. When the patient was threatened with the first he made no effort to guard himself or to withdraw his head, nor did he show any instinctive combative reaction. Similarly, he appeared to be quite disinterested when a match was struck close to his face or eyes. He showed the same lack of reaction to unexpectedly loud noises or strong flashes of light. This corresponded to the failure to react to unexpected and dangerous acoustic stimuli referred to above.

The patient soon discovered that the examiners were interested in the way he reacted to painful stimuli. He accordingly tried to explain his reactions by such expressions as: " I am not a man who cannot stand pain," or " I am used to that because I have worked on the road," or " Labourers are always hurting themselves; we don't take any notice of it." On the other hand, his wife assured us that he had always been susceptible to pain and had reacted violently whenever his children pricked or pinched him in play.

Physical State.—General condition: well-built, muscular man, showing an old appendicectomy scar. Heart and arteries normal. Blood pressure 160/110. Small degree of emphysema, lungs otherwise healthy. Small epigastric hernia. Other systems normal. Urine normal. Wassermann and Meinicke reactions in blood normal.

Skull.—Moderate tenderness, most marked on the left temporal region. X-ray examination: fine crack in the squamous part of the left temporal bone, running upwards and slightly backwards through the middle of the squama for about 2 in. A skiagram taken two months later showed a faint crack in the left petrous bone.

Eyes.—Left eye blind (cataract). Right eye, normal vision, visual field normal, reaction of the pupil to light and convergence normal.

Otological Findings.—The results of the audiometer test have been reported above. The usual examination with tuning forks showed no abnormality. Labyrinthine investigations: no spontaneous nystagmus, no vertigo, no tendency to fall, Barany's pointing test normal. Examination on the rotating stool revealed normal, but obviously

reduced reactions. Syringing produced normal reactions on the right ear, reduced reactions of a normal type on the left side.

Central Nervous System.—Cranial nerves showed no pathological signs, apart from those above mentioned. Trunk: abdominal reflex present and equal. Muscular power normal. Upper extremities: tendon reflexes brisk on both sides. Muscular power, tonus, all forms of sensibility, normal; no ataxia. Lower extremities: knee and ankle-jerks exaggerated. Variable patellar clonus on the right side, no ankle clonus, no extensor plantar reflex. Oppenheim's sign negative. No disorder of muscular power and of tonus. All forms of sensibility normal. No ataxia. Romberg's sign negative. Gait: patient walks on a wide base rather clumsily, but without definite ataxia.

Summary of the case history

A man of 34 was admitted to hospital following a serious head injury. When the concussion had subsided, he showed a disturbance of understanding of spoken language. There was no other sign of a gross abnormality of the central nervous system. X-ray examination revealed a fissure of the left squama ossis temporalis and a faint crack of the left temporal bone. There was a reduced reaction to left-sided labyrinthine stimuli. The hearing proper was intact except for a slight impairment of appreciating high tones with the left ear. The patient stated that he could hear noises, but could not understand spoken language. He said spoken language sounded as strange, as if he were hearing a foreign language unknown to him. It was amply proved that what the patient heard differed considerably from the normal sounds of speech. The patient could not hear spoken words correctly, nor could he write to dictation. There were no other signs of speech disorder apart from a certain logorrhœa in the early stages of the illness.

His reaction to unexpected acoustic stimuli was inadequate. He did not show the normal reactions of turning away from or towards the source of sounds, but there was no disorder of attention during conversation. Also he did not show the normal reactions of withdrawal and defence to painful stimuli, nor to visual stimuli which usually give rise to such reactions, nor did he respond adequately to warnings of danger. At the same time, there was no disturbance of sensibility. The patient tried to rationalize this lack of reactions. During the time of observation, extending over half a year, the symptoms did not change materially.

Diagnosis.—The prominent features of this case corresponded with the pure word-deafness as described by Lichtheim. The inability to perceive spoken words correctly, as observed in this patient, has been shown in many cases and has given rise to the term "word-sound-deafness." Besides the pure word-deafness, there was a second symptom, first described by Schilder and Stengel in 1928 as "asymbolia for pain." This symptom consists in lack of adequate reactions to painful stimuli which are obviously perceived correctly by the patient as pain. As in other cases showing this symptom, he also lacked the appropriate reactions to strong acoustic and visual stimuli unexpectedly applied. The diagnosis, therefore, is one of pure word-deafness combined with asymbolia for pain.

Discussion

The case described belongs to that group of cases of pure word-deafness in which the inner language is totally unaffected. It has been shown that the very slight lesion of the auditory apparatus cannot be held responsible for the symptom of pure word-deafness. Our case seems to confirm what others have suggested, that in a number of the cases of pure word-deafness there is some defect of the auditory apparatus. One finds the cases mentioned in the literature falling into two groups, namely, those that have developed from an auditory aphasia and those that have not. We cannot say with certainty to which group our patient belonged, for obviously examination was not possible in the early days after his accident, so that one cannot entirely exclude the possibility that an auditory aphasia existed for some days first. In this connection it was noted that the patient exhibited a volubility reminiscent of a logorrhœa, which might be regarded as being the last trace of an auditory aphasia. His tendency to repeat questions and commands is similar to what can be observed in the stages of recovery of pure echolalia in aphasics.

As in cases described by others, our patient showed that he could not perceive words naturally. But, as we have shown in the description of the case, this aberration of perception is totally different from what is found in an ordinary deaf person. The very slight loss of hearing as found in our patient by itself would never have caused such distortion of heard language as he evidently experienced. Our patient described what he heard as something strange and unnatural, but he insisted and proved that he could hear, and his whole attitude was different from that of a deaf person. Hoff and Silbermann (1933) have found that certain patients suffering from lesions of the left temporal lobe complained that heard speech had a strange quality not experienced by them before the illness, which the authors were prompted to name "depersonalization of language." This is reminiscent of what our patient described himself.

The physical examination suggested a slight affection of the left labyrinth. The tinnitus was in keeping with a lesion of this sort, as was the result of the audiometer test. However, similar tracings with the audiometer are obtained where the lesion is in the temporal lobe (Silbermann and Tamari, 1937). The presence of tinnitus in itself cannot be regarded as symptomatic of lesions of the labyrinth, as Frazier and Rowe (1934) have shown. It was present in the majority of their 53 cases with verified tumours of the temporal lobe. It is therefore possible that there was a lesion of the left temporal lobe (as has been found in many cases of pure word-deafness), co-existing with that of the labyrinth. The fact that a fissure through the middle of the squama of the left temporal bone could be demonstrated also points to this possibility, as this fissure extended to the level of the middle of the first temporal convolution, where lesions have been found in pure word-deafness. It is, therefore, not unreasonable to conceive the possibility of there being a cortical lesion causing the pure word-deafness, more especially as the other symptom of the case can only be explained by a cortical lesion. Once more it is important to remember

the lesson taught by Freund's case, where the clinical observer first tried to attribute the pure word-deafness to the existing labyrinthine lesion alone, but where the post-mortem examination revealed that a left-sided temperosphenoidal tumour was the real cause of the symptom. From this experience we learn that in trying to explain a rare clinical event, such as pure word-deafness, we need not shrink from assuming an uncommon combination of causes.

Besides the pure word-deafness a second important symptom has been described in our patient: this is what has been called asymbolia for pain. This symptom consists in a loss of adequate reactions to painful and other sudden stimuli, such as a loud noise or a flash of light. The patients so described showed no disturbance of sensibility, but they failed to make the usual efforts of withdrawal or defence. Some of them even showed a paradoxical reaction in which the reactive movement was in the direction of the source of a danger that a normal individual would instinctively associate with a pain suddenly inflicted on the body from without, or an unexpected loud noise or a flash of light. As pointed out by Schilder and Stengel (1928), this behaviour bears a resemblance to some of the reactive movements seen in catatonic conditions. It is, of course, not suggested that any causative factor common to both conditions can be assumed. It could be argued, perhaps, that what has been called asymbolia for pain is nothing but an hysterical phenomenon, especially if it follows an accident. However, the symptom has been undeniably demonstrated in cases where there were gross organic lesions of the brain with a certain consistent localization. This symptom does not resemble any recognized hysterical manifestation and it differs markedly from the hysterical anæsthesias in that in this case the patient insists that his feeling is intact and endeavours to deny or explain away his abnormality. This behaviour is essentially opposed to the attitude of the hysteric, who prefers to demonstrate his disability.

In a number of cases asymbolia for pain has been observed combined with auditory aphasia and only in a few cases without this complication. Potzl and Stengel (1937) have reported a case in which asymbolia for pain was associated with the so-called conductionaphasia, i.e. a form of auditory aphasia in which an ability to repeat heard words is prominent. It is of interest that both conduction aphasia and pure word-deafness have been regarded as stages in the recovery from auditory aphasia. There is certainly in both these conditions the common feature that the ability to repeat words is impaired or destroyed. However, the inner language is intact in pure word-deafness and impaired in conduction aphasia.

One feature in the symptomatology of pure word-deafness is of particular interest in connection with asymbolia for pain. That is the lack of reaction to auditory stimuli. This feature has been considered as due to a lack of attention. We have pointed out that such an interpretation is not correct. In reality these patients are not unattentive in conversation. On the contrary, they are anxious to catch every word and the meaning of every word as soon as they are engaged in conversation. What is really lacking is not the ability to attend, but the reflex turning towards the person speaking or the origin of the noise. This deficiency at once suggests a relation to the lack of adequate reaction to painful,

visual, and auditory stimuli, characteristic of asymbolia for pain. One is justified in saying that pure word-deafness contains one important feature of asymbolia for pain, and vice versa. This common feature seems to be a lack of the ability to make an appropriate response to stimuli reaching the patient from the outer world. One can maintain that asymbolia for pain is the more primitive and more general symptom, while the lack of response in pure word-deafness is confined to one special group of stimuli.

For the understanding of asymbolia for pain from a biological point of view, it is necessary to note that in the majority of cases asymbolia for pain is combined with some form of word-deafness. All types of word-deafness represent, after all, a loss of relation to the outer world, confined to the lack of understanding of spoken language. The combination of these two symptoms is certainly not accidental, but indicates a deep relation between them, formed by the common loss of certain reactions in human behaviour, biologically important. It was pointed out that in asymbolia for pain the reaction to dangerous stimuli may be either entirely lacking or impaired, although there is no impairment of perception of stimuli. The same seems to be true for pure word-deafness in the acoustic sphere. The failure of our patient, as we have reported, to react adequately to an acoustic warning signal in a situation experienced every day in normal life (we refer to his disregard of a motor horn) shows how vital are the reactions which the patient has lost. For our case it cannot be definitely decided whether this loss of flight reaction was due to the pure word-deafness or the asymbolia for pain. Either condition could be held responsible. This behaviour differs entirely from what is observed in ordinary deafness, where the individual is anxious to respond to every audible sound and indeed tends to react in an exaggerated way to heard warning stimuli. It is difficult to estimate how rare is the combination of pure word-deafness with asymbolia for pain. In the cases reported in the literature there is no evidence to show that the latter symptom was investigated.

As to the site of the lesions responsible for the symptoms in our patient, we are unable to make a definite statement. We have already shown that there was probably a lesion of the left labyrinth which by itself could not explain the pure word-deafness. It is necessary to assume the existence of a cortical lesion. According to the literature, lesions of the middle part of the first temporal convolution of the left hemisphere adjacent to the auditory cortex of Heschl's transverse convolution, have been found in pure word-deafness (Bonvicini, 1905; Liepmann, 1908; Gehuchten and Goris, 1910; Potzl, 1919; Henschen, 1923; Schuster and Taterka, 1926; Goldstein, 1927; Kleist, 1934). These lesions were said to have severed the connection between that part of the first temporal convolution and the auditory cortex. There is no measure of agreement as to what extent the auditory area itself is involved and to what degree the middle part of the first temporal convolution can be regarded as belonging functionally to the auditory area. However, it is significant that in our case there was a traumatic fissure of the left squama ossis temporalis, projecting over the " word-deafness region." There were no signs suggesting a bilateral cortical lesion such as others have reported.

The existence of asymbolia for pain suggests in itself a certain localization. In a number of cases described the post-mortem examination consistently revealed lesions of the supramarginal gyrus of the left side (Schilder and Stengel, 1928; Potzl and Stengel, 1937). In our case we feel tempted to assume an involvement of this area. Kleist (1934) has described a case of pure word-deafness where a lesion of the left temporal convolution existed with a lesion of the supramarginal gyrus, indicating that such a combination does occur.

The precise nature of the lesion itself cannot be ascertained, but there was undoubtedly a severe trauma to the brain associated with a fracture of part of the temporal bone. It can be assumed that the trauma was followed by a hæmorrhage on or into the substance of the brain. The patient's blood pressure being somewhat high, it is possible that small vessels near the surface of the brain may have been ruptured.

The question of the pure word-deafness in the scheme of aphasias can now be discussed. The answer to this question naturally is bound up with the very definition of aphasia in general. If, according to Head, aphasia is defined as " a lack of the capacity of symbolic formulation and expression," one can hardly regard pure word-deafness as an aphasic disorder. If the disturbance of the inner language is made an essential condition for regarding a speech disorder as an aphasia, pure word-deafness must be rejected from the scheme of aphasia on these grounds. It seems as if the disturbance essential for pure word-deafness involves a function of perception of a higher level than the hearing proper. The supposition that the middle part of the first left temporal convolution, usually involved in pure word-deafness, is to be regarded as an extension of the auditory sensory area (Henschen, 1923), supports the idea that the function lost in pure word-deafness is something which is of a sensory character, although indispensable for understanding of spoken language. Whether one regards this function as part of the speech mechanism or as part of the perceptive sensory process is a theoretical question. The fact that pure word-deafness has been observed in the course of the recovery of a typical auditory aphasia does not determine this question one way or the other. Against the assumption that such a fact is a proof that pure word-deafness represents only a stage in auditory aphasia, it could be argued with equal justice that by the recovery of the auditory aphasia the other symptom is permitted to appear on the surface. In the same way the relationship between auditory aphasia and conduction aphasia could be explained. In conduction aphasia an element of a more peripheral character appears to complicate an auditory aphasia (Stengel, 1933).

Summary

A case has been described in which there was a syndrome consisting of pure word-deafness and what has been described as asymbolia for pain, following a head injury. The inter-relationship of these two disorders has been discussed and it has been pointed out that pure word-deafness and asymbolia for pain have the common feature of a disturbance in the relationship between the individual and his environment. The localization of the responsible lesions has been

discussed. Consideration has been given to the problem of the position of pure word-deafness in the systems of aphasias.

We wish to express our gratitude to Dr. J. J. B. Martin, Medical Superintendent of the Bristol City and County Mental Hospital, for permission to publish this case; to Dr. A. J. Wright, Honorary Surgeon to the Ear, Nose and Throat Department of the Bristol General Hospital, for placing the otological findings at our disposal; and to Dr. H. H. Carleton, Honorary Physician to Bristol General Hospital, for giving us the opportunity to examine this case while under his care.

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NEURONAL DIFFERENTIATION IN IMPLANTED FŒTAL CORTICAL TISSUE

BY

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(RECEIVED 7TH MARCH, 1940)

THE capacity for continued growth and differentiation, up to a certain point, of grafted fragments of the embryonic nervous system has been amply demonstrated in lower vertebrates. In the chick, for example, it has been shown that if segments of the spinal cord anlage are implanted on the allantois, the cells of the neural plate show high powers of proliferation and typical nerve-cells with abundant processes are formed (Danchakoff and Agassiz, 1924). In the cord the three layers—ependymal, mantle, and marginal—are developed, and the neuroblasts of the mantle layer become arranged in groups resembling the ventral and dorsal horns of grey matter in the normal cord. Similar powers of differentiation were found by Hoadley (1924) in portions of the embryonic mesencephalon of chicks of 48 hours' incubation, which had been grafted on the chorio-allantoic membrane. The roof of the mesencephalon acquired a laminated structure similar to that which is characteristic of the tectum opticum of a normal 8-day chick, with outer and inner cell layers and outer and inner fibre layers.

As regards mammalian tissues, the differentiation of transplanted primordia of the eye and ear of rabbit embryos grafted on to the omentum has been demonstrated by Waterman (1932). The various layers of the retina (nuclear layer, inner reticular layer, ganglion-cell layer, and nerve-fibre layer) can all be recognized, and the optic nerve also commences its development. In the otic primordia the maculæ and cristæ acousticæ of the labyrinth appear, sometimes associated with identifiable ganglion-cells and nerve-fibres. Continued growth of nervous tissues has also been observed in total or partial transplants of rat embryos which have been grafted on to the chick chorio-allantois (Nicholas and Rudwick, 1933). Thus the ectoderm of the medullary plate may form the main subdivisions of the central nervous system, including a well-developed neural tube and vesiculation of the cerebral region. Diencephalic diverticula may appear and the mesencephalon may show a characteristic thickening of the roof. Nerve-fibres wander out from the cord to end blindly in the surrounding

mesenchyme, and the cellular arrangement inside the cord for a time proceeds normally in its differentiation.

In none of these experiments has any attempt been made to determine how far individual neurones in different parts of the brain can proceed in their differentiation towards the attainment of the cytological characters of the corresponding mature nerve-cells.

The present investigation of the capacity for self-differentiation of mammalian cerebral cortex was initiated by a consideration of its relative structural independence of connections with other parts of the brain. In 1911 Nissl reported that if portions of the cerebral cortex are separated from subcortical centres in young rabbits, some cell atrophy occurs in the infragranular layers. On the other hand, the superficial layers of the cortex show very little change —indeed, they may even undergo further development. In a recent study of the visual cortex in the macaque monkey (Le Gros Clark and Sunderland, 1939) it was found that isolation from other parts of the brain led to remarkably little change, except for the atrophy of certain large cells of the granular and infragranular layers, a slight " thinning-out " of cells of all the layers, and the disappearance of certain fibres. It thus appeared that most of the cells of the visual cortex comprise an intrinsic cortical mechanism which is not dependent for its normal existence and organization on connections with other parts of the brain.

In considering the most suitable medium for the implantation of fragments of embryonic cortex, the brain of young animals naturally suggested itself, since this tissue may be presumed to supply an appropriate nutritional environment for the graft. Intracerebral implantation has been employed by previous investigators for the study of the growth and differentiation of embryonic tissues, but the earlier reports on this method were not encouraging. del Conte (1907) concluded that in dogs brain tissue was definitely unfavourable for such transplants, and he supposed this to be due either to the adverse influence of certain cellular elements in the brain or to the sparsity of blood-vessels in the white matter. However, he obtained good results with the intracerebral implantation of pituitary tissue. Tiesenhausen (1909), in a comprehensive study of the implantation of fœtal tissues in fowls, also found practically no success with grafts inserted into the brain. More recently, however, the method has been used with excellent results by Willis (1935) in the case of rat embryos. He injected minced tissues derived from rat embryos ranging from the earliest phases of gestation up to the 3·5-cm. stage into the cerebral hemispheres of young rats, and in many experiments he obtained the survival and growth of tissues of various kinds. In no case, however, did he find in the implants any surviving structures of the central nervous system. However, it seems probable that the survival of neuroblastic tissue in these grafts may have been prevented by the proliferative activity of mesodermal tissues introduced at the same time.

In the present study rabbit embryos of 15 to 20 days were used and portions of fœtal cortex were freed from their mesodermal coverings before being implanted as isolated fragments into the cerebral hemispheres of young rabbits.

Methods

Under ether anæsthesia and with a strictly aseptic routine the rabbit embryos were removed from the uterine cornua and placed in sterile saline solution. With the aid of a binocular microscope and fine ophthalmic instruments, the skin and the subjacent mesodermal tissues were stripped off the surface of the fœtal brain. Fragments of the exposed cortical surface of the cerebral hemispheres were then excised and placed in sterile saline in an incubator while preparations were made for their implantation.

The host animals were young rabbits aged about six weeks. Under ether anæsthesia and with an aseptic operative technique, the roof of the skull was exposed by a longitudinal skin incision, a small trephine hole was made over the frontal region of one cerebral hemisphere, and the dura mater opened. For the insertion of the fœtal cortical tissue a sternal puncture needle with a bore of 2·2 mm. was employed. The usual pattern was modified by bluntly bevelling the end and by providing it with an accurately fitting plunger which, when pushed home, projects 1 mm. beyond the open end of the needle. A fragment of fœtal cortex was placed just within the lumen of the needle and the latter was then introduced obliquely through the trephine hole and pushed into the brain of the host until (as judged by previous dissections) it had reached the cavity of the lateral ventricle. The plunger was then pushed home and the needle withdrawn. The slight degree of venous hæmorrhage from the brain which usually followed this procedure was easily arrested by the local application of a pledget of cotton-wool soaked in hot saline. The scalp wound was closed with sutures.

The host rabbits were killed about four weeks after the operation. In each case the brain was removed immediately after death and the hemisphere containing the implanted tissue placed in 70 per cent. alcohol. After fixation for 2 days the region of the implantation was exposed by a coronal incision and the cut surface inspected with a binocular microscope. Suitably trimmed blocks were then prepared, embedded in paraffin, and sectioned serially at a thickness of 15μ. Alternate sections were stained with Borell's methylene blue and Bodian's protargol technique, thus providing the material for a correlated study of cellular architecture and fibre pattern.

In many of these experiments the implanted neuroblastic tissue had survived and had undergone some degree of growth and differentiation. This was usually most marked in the wall of the lateral ventricle, though in some cases masses of nervous tissue had also developed near the base of the brain in the region of the tuberculum olfactorium.

Results

On first inspection of the serial sections in the successful experiments, the most striking feature of the grafted tissue is the degree to which individual neurones had undergone cytological differentiation, and the present report is primarily concerned with this phenomenon. The neuronal differentiation may best be described by reference to one experiment (rabbit 62) in which a circumscribed mass of neural tissue had grown in the hippocampus and fornix where these structures project into the cavity of the anterior part of the lateral ventricle. In this instance a fragment of cortex from a 15-day embryo was implanted in the brain of a 6-weeks-old rabbit on 9th September, 1939, and the animal was killed 32 days later. If the cells of the implanted tissue had continued to grow and undergo differentiation at the normal rate, therefore, they would be expected to have reached a stage of development equivalent to that of an 18-days-old rabbit.

In Fig. 1 is shown a photomicrograph of a coronal section through the

lateral ventricle and hippocampus of rabbit 62, which illustrates the general appearance of the implanted tissue under a low-power objective. It has established itself in the substance of the hippocampus and dorsally it forms a surface eminence bulging into the cavity of the lateral ventricle. Below it extends into the column of the fornix, and here it also forms a surface eminence on its lateral aspect.

The nerve-cells of the implant show a definite grouping and they have clearly undergone a segregation in relation to their cell-type. Clusters of large

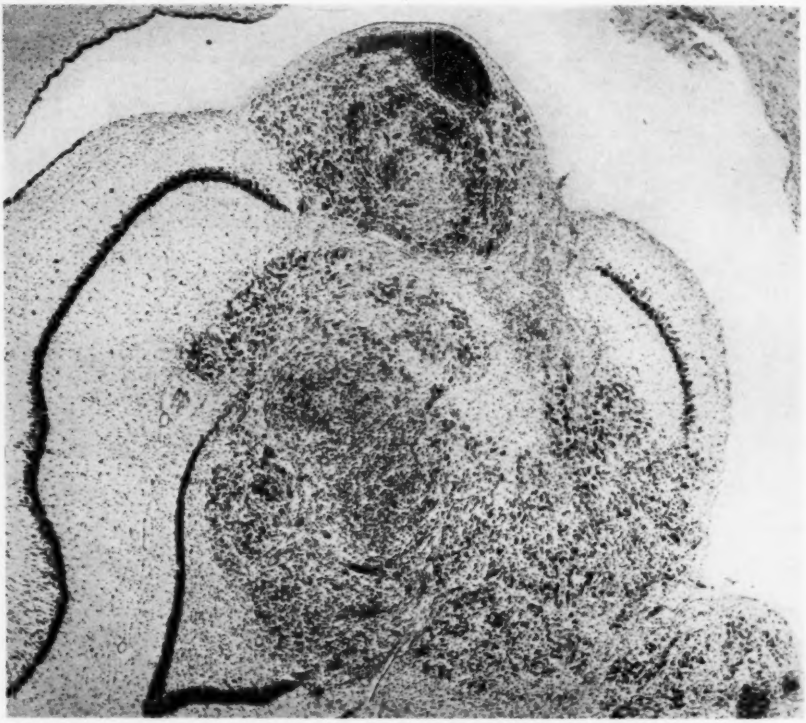


Fig. 1.—Coronal section through the lateral ventricle and hippocampal formation of rabbit 62, showing the mass of nervous tissue developed from implanted fœtal cortex. Borell's methylene blue ; × 30.

cells are distinctly segregated from groups of medium-sized and small cells, and sometimes demarcated by relatively acellular zones. The arrangement of the cells in each group shows considerable variation. They may form an irregular clump, but not infrequently they are disposed in whorls or in a somewhat indistinct laminar formation. The latter is of particular interest, since a laminar pattern is characteristic of the normally developed cerebral cortex.

Before describing the neuronal differentiation in the implanted tissue,

reference should be made to the structure of the normal embryonic cortex. In a rabbit embryo of 15 days (of which a borax-carmine series of sections was available for study), the cerebral cortex on the lateral surface of the hemisphere shows almost no differentiation (Fig. 2*a*). A continuous layer of neuroblasts,

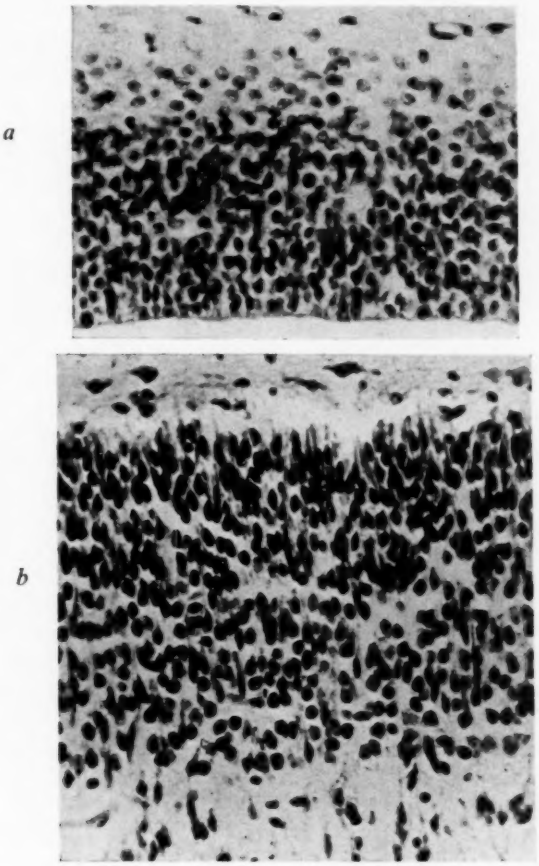


Fig. 2.—(*a*) Section of cerebral cortex of a 15-day rabbit embryo. The cavity of the lateral ventricle is below. Borax carmine; ×350. (*b*) Section of the cortical layer of cells in a 20-day rabbit embryo. Above is the zonal layer of the cortex ; below is seen the superficial part of the intermediate zone of the wall of the cerebral vesicle. Borell's methylene blue ; ×350.

the germinal layer, extends from the cavity of the lateral ventricle towards the surface of the brain. At the surface is a thin marginal layer. The neuroblasts are rounded or oval in shape, with a relatively large, lightly staining nucleus and a minimal amount of cytoplasm. With ordinary staining methods no cell-processes are visible. Mitoses can be seen throughout almost the whole thickness of the cortex, but they are more abundant among the deeper

cells near the ventricular cavity. At this stage there is no differentiation of the cortical cells into layers except in so far as the most superficial cells are almost free of mitotic figures.

At 20 days the cortex has already undergone some differentiation (Fig. 2*b*), for a cortical layer of cells has now become separated from the germinal layer by an intermediate zone in which neuroblastic cells are relatively few and scattered. The cortical layer has a thickness of 0·15 mm. and consists of densely packed neuroblasts, many of which have assumed a pyramidal form with a well-marked apical process. In silver-stained preparations this process can be traced for some distance towards the marginal layer on the surface of the cortex. No basal dendrites are visible, though their incipient development is in some cases indicated by an angulation of the basal part of the cell. The developing pyramidal cells have nuclei which are oval and darkly staining, and among them are numerous neuroblasts of a more embryonic type. These are rounded or oval cells with larger, more rounded, and more lightly staining nuclei, and they show no visible processes. There is as yet no apparent stratification of the cells of the cortical layer.

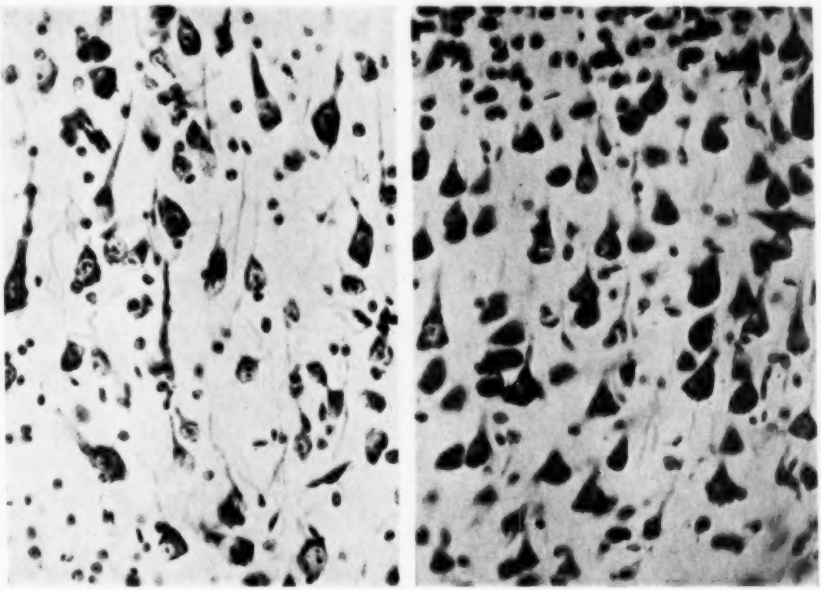
In the intermediate zone, which separates the cortical layer of cells from the germinal layer of the ependymal zone, are scattered fusiform cells with elongated, narrow nuclei, and fine protoplasmic processes which are for the most part directed towards the surface. In their general character and arrangement, and in their relation to the subjacent germinal layer, these cells recall the appearance of cells migrating out from the margin of explanted fibroblastic tissue ; indeed, such a movement of cells is commonly presumed to occur in the process of development and differentiation of the cortex. The neuroblasts produced by the proliferative activity of the germinal layer are described as migrating superficially to take part in the formation of the cortical layer of cells. However, no active amœboid movement has been directly demonstrated in the cells of the intermediate zone, though their general appearance in sectioned material and the morphological contrast which they show to the cells of the cortical layer and the germinal layer suggest that this may indeed be the case.

In the germinal matrix of the cortex of the 20-day rabbit embryo the neuroblasts are very closely packed together. Mitoses are frequently to be seen in the cells which lie alongside the ventricular cavity, and the most superficial cells become elongated and send fine protoplasmic processes up into the intermediate layer.

In the implanted cortex of rabbit 62, pyramidal cells typical of those found in the normal mature cortex are plentiful. They may reach a width of 15–20μ at their base and they give off stout apical dendrites which, even in methylene blue sections, can often be followed for a considerable distance. A group of these cortical pyramidal cells is shown in Fig. 3*a*, and for comparison the pyramidal cells from the infragranular layers of the limbic area of the cortex of a 3-weeks-old rabbit are shown in Fig. 3*b* (at the same magnification). It will be observed that in respect of size and differentiation the comparison is very close. In the photomicrograph of the implanted cortex the pyramidal cells are in general orientated in the same direction ; they show the normal

content and arrangement of Nissl substance (which may extend for some way along the apical process), and the nucleus is quite normal in appearance. In many cells the apical dendrite can be seen to give off collaterals at approximately right angles and to end in a terminal dichotomization. Basal dendrites are also frequently quite evident, extending laterally from the basal angles of the pyramidal cell.

In the protargol sections the pyramidal cells do not stand out as conspicuously as in the methylene blue sections. The cell-bodies are not impregnated as deeply as the pyramidal cells in the cortex of the host brain.



a *b*

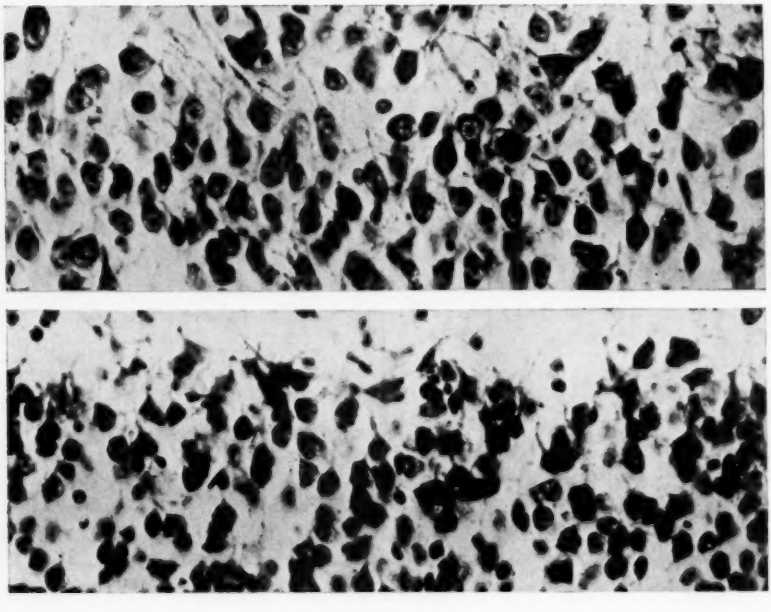
Fig. 3.—(*a*) Large pyramidal cells of cortical type from the implanted tissue in rabbit 62. Borell's methylene blue ; ×350. (*b*) Large pyramidal cells from the infragranular layer of the limbic area of the cortex in a 3-weeks-old rabbit, for comparison with Fig. 3*a*. Borell's methylene blue ; ×350.

Nevertheless, many of them show a distinct neurofibrillar structure. The apical dendrites and in some cases the basal dendrites also are more heavily impregnated and in their proximal portions they may show exceptionally clear neurofibrillæ.

It has been noted that some groups of pyramidal cells show a fairly regular orientation so that their apical processes extend in the same direction. This is by no means always the case, however, for in other groups the pyramidal cells may be irregularly disposed in a manner which is apparently quite haphazard. Where a whorl arrangement of cells is present the apical processes are commonly directed towards the centre of the formation. In other cases

it may be observed that the apical processes extend towards a zone of smaller cells which present a striking similarity to the more superficially placed cells of the normal mature cortex. In other words, a type of lamination characteristic of the mature cortex is reproduced. These smaller cells are characteristically closely packed together, and in their arrangement and morphology they may be compared to the lamina granularis externa—particularly of the limbic areas of the cortex. In Fig. 4*a* is shown a photomicrograph of such cells in the implanted tissue, and for comparison (at the same magnification) the cells of the

a



b

Fig. 4.—(*a*) Group of small cells of cortical type from the implanted tissue in rabbit 62. Borell's methylene blue ; ×350. (*b*) Cells of the lamina granularis externa from the cortex of a 3-weeks-old rabbit, for comparison with Fig. 4*a*. Borell's methylene blue ; ×350.

lamina granularis externa of a 3-weeks-old rabbit are shown in Fig. 4*b*. In the latter they are seen to be rounded or sub-triangular and to give off short apical processes which undergo a rapid dichotomization, those of the more superficial cells ramifying in the lamina zonalis of the cortex. In the implanted cortical tissue the cells appear somewhat larger and they are less regularly arranged. They give off similar short dendritic processes, which are, in general, orientated in a common direction and ramify freely.

In other parts of the implanted tissue circumscribed groups of small nerve-cells are found closely packed together and resembling in their general appear-

ance the cells just described. They are somewhat smaller, however, and show no definite orientation. Their processes, also, are shorter and finer. They are quite similar in their morphology and disposition to the stellate cells of the lamina granularis interna of the adult cortex. Such a group of cells is shown towards the centre of the photomicrograph in Fig. 1.

In the protargol sections most of the cell groups of the implanted tissue are seen to be pervaded by a fine plexus of nerve fibres. In some areas, also, well-defined fasciculi are present among the groups, with a tendency to run circumferentially about a collection of cells where these are arranged in a whorl formation. Where the large pyramidal cells show a regular orientation the nerve-fibres may be loosely disposed in fasciculi which have the same direction as the apical processes of the pyramids, recalling the arrangement of the radial fibres in the adult cortex. The origin and destination of these fibres have yet to be traced.

In general the implantation and growth of fœtal tissue has provoked very little or no reaction in the host tissue. In some regions there are small areas of gliosis which are almost certainly due to local injury sustained during the operative procedure of implantation. In the implanted tissue itself local patches of dense neuroglial tissue are found, which are presumably derived from the proliferation of spongioblastic elements in the fœtal cortex. Such a patch is seen in the photomicrograph in Fig. 1 at the summit of the eminence which projects into the lateral ventricle from the dorsal surface of the hippocampus.

Discussion

The experiment recorded in this paper demonstrates the viability of cortical neuroblastic tissue which has been implanted into the brain of a young animal. It also demonstrates its capacity for continued growth and differentiation. In the implanted tissue are to be found fully differentiated neurones similar to those which are normally present in the different laminæ of the adult cortex. These neurones attain to their mature size and shape and they give rise to dendritic processes of a normal character. They show a segregation into groups in relation to their cell-type, and there is some evidence of an attempt at an organization comparable to that which is normally found in the mature cortex. It thus appears that the differentiation of cell-types can occur independently of the normal connections of the cortex with other parts of the central nervous system, and this is possibly also the case with their organization into the characteristic cortical laminæ. The common orientation of cells and their processes which is found in some groups in the implanted tissue may be an expression of an orientation which was already present in the cortex of the 15-day rabbit embryo and which was not disturbed in the course of implantation ; or it may be the result of some extrinsic influence or mutual interaction affecting the neuroblasts during their development in the host tissue. This raises a problem which requires further investigation by experimental embryological methods. It has been abundantly demonstrated from previous studies

of transplanted embryonic material and of the culture *in vitro* of nervous tissue that the outgrowth of cell-processes is dependent on an inherent capacity of the neuroblast and not on the establishment of a normal functional relation with other neurones or with effector mechanisms and sensory surfaces. The present observations lead to the inference that the differentiation and orientation of dendritic processes in cortical neurones are likewise not dependent upon influences related to an excitatory field to which the neuroblasts may be presumed to be exposed during their normal development.

Summary

Fragments of embryonic cortex removed from rabbit embryos and implanted into the brains of young rabbits continue to grow and to undergo differentiation.

Typical mature cortical neurones, characteristic of the various laminæ of the adult cortex are found. They show a tendency to organization in groups and laminæ similar to those which are normally formed in the development of the cortex.

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Therapeutic Quartan Malaria in the Treatment of Neurosyphilis among Negroes. G. C. Branche. 967.

Biochemistry of Epilepsy.—Is epilepsy a symptom of disturbed general physiology? Biochemical studies of blood of epileptics are described, as to sugar, acidity, alkali reserve, gases, Ca and P, nitrogenous substances, cholesterol, chlorides. Studies show a more than normal variability in epileptics; most have normal glucose tolerance curves. Frequency of seizures can be increased or decreased by alteration in chemical constituents of blood, though some of the changes noticed are the result, not the cause of fits. There is no evidence of intoxication with alkaline substances as cause of fits. Slight temporary acidosis during and after fit is due to increased muscular metabolism, *p*H normal in majority, no evidence of general cerebral anoxæmia. Epilepsy is not related to tetany. Fluctuations in blood Ca increases fluctuation of excitability in nervous tissue; blood fibrinogen is increased; most constant physiological abnormality is inconstancy. This applies to blood sugar level, *p*H, blood Ca, etc. (H. de P.)

E.E.G. and Schizophrenics.—A comparison of E.E.G. of 132 schizophrenic and normal subjects, in 4 groups. (1) Most normal E.E.G. of schizophrenic group are those of paranoids; (2) dysrhymic pattern not differing from those of non-schizophrenic with convulsive disorder (e.g. epilepsy) found in catatonics; (3) choppy pattern, suggesting irritation or other lesion may be due to organic disease; (4) mixed. Brain patterns change only when brain physiology changes. Work is still in progress and may be useful both for diagnosis and in deciding treatment in individual cases. (H. de P.)

E.E.G. in Psychoses.—Use of E.E.G. in localizing cerebral tumours, method adapted for localizing cerebral atrophy by testing for distribution of alpha wave activity in psychotics, simultaneous recording from two regions—normal and pathological—necessary for true comparison; method and results are described and discussed. (H. de P.)

Psychotic Manifestations in Cerebral Vascular Lesions.—Correlations between acute cerebral lesions and psychotic manifestations were recorded in 170 out of 1000 cases, all severe, ending fatally in a short time. Cortical destruction caused larger proportion of psychotic symptoms than involvement of basal ganglia by perforating vessels. (H. de P.)

Menopausal Depression and Estrogenic Hormone.—Investigations on depressed patients of menopausal and post-menopausal age groups are described. Character and severity of symptoms varied somewhat, but all required in-patient treatment. They received œstrogenic hormone while being treated by psychotherapy, recreation, etc. Beneficial effects were confined to improvement of vasomotor symptoms and general well-being. Œstrogenic hormone does not appear to be a specific therapeutic agent in severe depressions. (H. de P.)

Detoxication of Sodium Benzoate.—Quick's liver-function test based on excretion of hippuric acid after ingestion of benzoic acid has been applied to 18 patients with catatonic dementia præcox. Results suggested that metabolic disturbance of the liver may be a characteristic feature of this condition. A modification of this technique was used on cases of this and other neuropsychiatric disorders; results suggest failure of absorption not due to hepatic dysfunction as the true explanation of these findings. (H. de P.)

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Folie à Deux : Report of a Case of Remission from a Psychosis of more than Twenty-Five Years' Duration. B. Postle. 372.

Experimental Disseminated Encephalopathy.—Seven monkeys were given inoculations for a period varying from four to thirteen months with sterile extract and emulsion of rabbit brain. A progressive condition, characterized by symptoms of wide-spread involvement of the central nervous system, developed. Pathological examination showed disseminated perivascular lesions characterized by destruction of myelin and accumulations of fatty granular cells. The macroglia at times had degenerated and at other times showed proliferative changes. In addition, large areas of partial demyelination which showed no apparent relation to blood vessels were observed. The pathogenesis of this experimental encephalopathy is investigated and its significance is briefly discussed in relation to similar conditions in man. (R. M. S.)

Pick's Disease with Temporal Lobe Atrophy.—The authors report a case of Pick's disease in which the focal atrophy was almost exclusively limited to the temporal lobes. The case is analyzed and an attempt made to correlate the clinical and pathological findings. (R. M. S.)

CO_2 Content of Blood in Epilepsy.—The authors' observations are consistent with electroencephalographic evidence that the type of cerebral dysrhythmia present in grand mal seizures is in contrast to that in petit mal attacks, and that carbon dioxide has a pronounced influence on cortical rhythms. All the available evidence indicates that carbon dioxide plays a significant etiological role in epilepsy. (R. M. S.)

Acid-Base Balance and Overventilation in Epilepsy.—The person with petit mal epilepsy responds to overventilation with a greater drop in the carbon dioxide content of the internal jugular blood and maintains the low level reached for a longer period after the overbreathing has ceased than does the non-epileptic control subject. The corresponding changes in the acid-base balance are such that the epileptic patient has an acid-base loop of greater area than the control subject. These findings can be explained on the assumption that the mechanisms which regulate the physicochemical state of the fluids of the brain are somewhat impaired in petit mal epilepsy, so that the person with such a condition is not able adequately to control or quickly adjust the acid-base balance when it is disturbed by overventilation. (R. M. S.)

Physiology in Concussion.—Animal studies were undertaken to determine the mechanisms operating in sudden loss of consciousness following blows to the head. It is suggested that the loss of consciousness as a result of a blow on the head may possibly be explained on the basis of short lasting, complete cerebral anæmia (Cannon). It is agreed with Weiss and Baker that the rate of circulatory change is important in the production of unconsciousness. (R. M. S.)

Spinothalamic Tract.—The course of the spinothalamic tract is traced from the apical and pericorneal cells of the posterior horn across the anterior commissure to the anterolateral columns. It then ascends in this column, its fibres gradually being pushed dorsad, so that just above the pyramidal decussation it lies immediately below the spinal tract of the fifth nerve. In the bulb it lies on the periphery and dorsolateral to the inferior olivary nucleus. Through the pons the spinothalamic tract is just medial to the middle cerebellar peduncle and on the same plane, but lateral to the medial lemniscus. In the mesencephalon it becomes peripheral again, lying just lateral to the brachium conjunctivum. It passes through the colliculi, to which the spinotectal fibres are given off, and then, lying just medial to the brachium of the inferior colliculus it enters the diencephalon. Turning abruptly laterad, the fibres of the spinothalamic tract terminate in the basal and ventral part of the nucleus ventralis posterior of the thalamus. There appears to be throughout the course of the tract a distinct, although probably somewhat overlapping, topical arrangement. (R. M. S.)

Flaccid Hemiplegia.—Clinical and pathological studies in man indicate that destruction of portions of the basal ganglia together with portions of the external and internal capsules may result in prolonged flaccid paralysis. The occurrence of flaccidity in man usually appears to depend on

the destruction of the striatum and its radiations. It is thought that the method of removing the hemisphere for glioma by first attending to the venous drainage before extirpation and clipping the large arteries as they are brought into view, offers the best clinical result because it spares the blood supply to the basal ganglia, although this method is probably more difficult and dangerous than that of first removing the arterial circulation. (R. M. S.)

Metrazol Shock and Schizophrenia.—The authors conclude that metrazol shock therapy does not seem to produce permanent and lasting recovery in schizophrenia. (R. M. S.)

Production of Headache with Subarachnoid and Ventricular Air.—It is suggested that the earlier phases of headache accompanying pneumoencephalography are not due to distortion of dural areas or the meningeal vascular tree. This type of headache is probably due to direct (chemical or mechanical) stimulation of the sensory nerve endings along many of the larger branches of the internal carotid artery. (R. M. S.)

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Spontaneous Hæmorrhage into Oculomotor Nerve with Rupture of Nerve and Fatal Subarachnoid Hæmorrhage. A. Plaut and M. Dreyfuss. 564.

Spread of Epileptic Discharge.—The after-discharge induced by electrical stimulations of the cortex is a faithful experimental counterpart of clinical types of epilepsy. Various motor variants have been observed which appear to be identical in their characteristics with those seen in certain clinical forms of epilepsy. The changes in blood flow in these monkeys during fits are the same as those seen in man during epileptic fits. The changes in electrical potential during and after epiliptiform fits are the same in monkeys as they are in man during epileptic seizures. A constant type of fit is easily reproducible in monkeys by electrical stimulation of the cortex. The corpus callosum plays a definite role in the spread of the epileptic discharge from one hemisphere to the other. Epileptic discharge from one hemisphere, if widespread over that cortex and prevented from spreading to the other hemisphere by section of the corpus callosum, gives rise to contralateral clonic movements and ipsilateral slow tonic movements, the latter being due, at least in part, to epileptic discharge from an area in the premotor region governing ipsilateral movements. Epileptic discharge of the neurons of the ipsilateral areas of the cerebral cortex gives rise to a large part of the tonic element of the convulsion. Transcortical section at right angles to the central sulcus, if it is of sufficient extent in a sagittal direction and of sufficient depth, alters the pathway for the spread of the epileptic discharge. With the cerebral cortex intact, subcortical centres play a secondary role in the spread of the epileptic discharge. The spread of the epileptic discharge takes place by neuronal pathways. (R. M. S.)

Anticonvulsant Properties of Sodium Diphenyl Hydantoinate.—Sodium diphenyl hydantoinate has anticonvulsant properties which are demonstrable by administration of metrazol subcutaneously in a group of epileptic patients before and after sodium diphenyl hydantoinate is given. (R. M. S.)

Heat-Regulatory Mechanisms.—In the chronic stage of the psychosis, schizophrenic patients show less reactivity to metabolic stimulation than do normal subjects. (R. M. S.)

Mineral Content of Brain.—Microincinerated sections of the brains of rabbits treated with either insulinor metrazol or a combination of the two, by a technique similar to that employed in the treatment of patients with psychoses, showed marked changes in the mineral content of the cerebral neurons. These changes consisted of dust formation, hypomineralization, vacuolation or complete demineralization of the ganglion cells. The changes were prominent in the cornu ammonis, but were also observed in other parts of the brain and appeared to correspond with those in sections stained with cresyl violet. Dust formation and complete demineralization

indicated severe damage to the protoplasm and could be observed as long as one hundred and seventeen days after completion of treatment. (R. M. S.)

Dissociation of Deep Sensibility at Different Levels.—Dissociated loss of postural and vibratory sensation was found to be not uncommon with lesions of the cerebrum, brain stem, and spinal cord. In seven patients with cerebral lesions causing disturbance of deep sensibility, position sense, stereognosis and two point discrimination were lost or markedly diminished, while the appreciation of vibration was spared or slightly affected. There were no instances in which the converse was true. With lesions at the thoracic and lumbar levels of the cord the opposite type of dissociation was found. Vibratory sense in the lower extremities was affected earlier and more severely than was the sense of position. In three patients with compression of the cervical region of the cord and medulla, with dissociated loss of deep sensation involving the upper extremities, sense of position was more affected than that of vibration, again with astereognosis. (R. M. S.)

Section of Spinal Root of Fifth Cranial Nerve.—Experience with the section of the bulbospinal root of the fifth cranial nerve and the results obtained from patients subjected to this procedure permit the following conclusions: (1) the operation is practical from the technical standpoint; (2) touch sensation of the face is preserved; (3) the subjective sensation of numbness is avoided; (4) the procedure is ideal for patients with malignant tumours of the face, since the exposure permits one to section the ninth cranial nerve as well as the upper cervical roots. (R. M. S.)

Colloid Cysts of Third Ventricle.—The most reasonable explanation of the origin of colloid cysts of the third ventricle is that they arise from the paraphysis, which is an embryonic structure derived from the fœtal ependyma of the anterior portion of the roof of the third ventricle. The histological structure of the cysts seems to substantiate this view, as tubules are frequently observed in their walls and suggest origin from a glandular structure. The symptoms are usually suggestive and when combined with evidence of blockage of one or both foramens of Monro, as shown in a ventriculogram and with other neurological findings indicating increased intracranial pressure and pressure on adjacent parts, make possible a pre-operative diagnosis with a fair degree of certainty. (R. M. S.)

Myoclonus Epilepsy.—In a case of myoclonus the central nervous system was studied histopathologically. Inclusion bodies, consisting of amyloid and argentophilic substances, with amitotic division in some, were observed throughout the nerve and glia cells of the central nervous system, except the spinal cord. The substantia nigra and the dentate nuclei were the main sites of these bodies. In correlating the clinical picture with the pathological changes the authors are inclined to attribute the mental symptoms to involvement of the cerebral convolutions, especially the frontal, and the so-called extrapyramidal symptoms to lesions in the substantia nigra. The myoclonus may possibly be due to the changes in the dentate mechanism, as in palatal myoclonus. (R. M. S.)

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Physiologic Regulation of the Cerebral Circulation. H. S. Forbes. 804.

Temporary Arrest of Circulation to C.N.S.—Twenty-four animals were subjected to periods of circulatory arrest, clamping of the pulmonary artery being used for this purpose. Arrest of the circulation for three minutes and ten seconds, or less, was tolerated without any obvious neurological disturbance. Subjected to three minutes and twenty-five seconds or more of circulatory arrest, cats showed permanent alteration in behaviour and psychic function. After six minutes of circulatory arrest vision and sensation suffered some degree of permanent injury. After seven minutes and thirty-six seconds of circulatory arrest there were permanent de-

mentia, blindness, serious sensory and auditory defects, motor and postural defects and reflex abnormalities. When the circulation was interrupted for eight minutes and forty-five seconds or longer, life could not be restored for more than a few hours. (R. M. S.)

Tuberculoma of Brain.—Tuberculomas of the brain occur at all ages and in a variety of types. With a few exceptions, they arise by hæmatogenous metastasis from a tuberculous focus elsewhere in the body, usually in the lungs or related lymph nodes. Clinical and pathologic studies indicate that tuberculomas producing the symptoms of tumor of the brain develop most frequently in adolescents and young adults with a single extracranial tuberculous focus. Tuberculomas associated with tuberculous meningitis tend to occur chiefly in children and in the presence of generalized tuberculosis. The pathological characteristics of tuberculomas are not different from those of tuberculosis elsewhere. Tuberculomas may be positively identified by finding acid-fast bacilli in them. Tuberculomas constitute only a small and declining percentage of verified tumours of the brain. The clinical syndromes which they produce are not significantly different from those produced by other varieties of cerebral tumour. A correct etiological diagnosis is made only when the patient has active tuberculosis in another organ or in the presence of a positive tuberculin reaction in a child. A history of tuberculous disease in the past is suggestive but not conclusive. Laboratory studies do not aid in the differential diagnosis. (R. M. S.)

Dystrophia Myotonica.—On the basis of the similarities of the properties of myotonia to those of Tiegel's, veratrine, neuromuscular and acetylcholine contractures, it is suggested that myotonia is a contracture and that the defect in myotonia is chiefly or entirely in the muscle. Evidence is presented that a defect in neuromuscular transmission does not adequately explain the observed phenomena and is probably not present. (R. M. S.)

Metrazol Convulsions.—Although local cerebral vasoconstriction may immediately precede a metrazol convulsion, there is no evidence from these studies that cerebral anæmia initiates the seizure. As the convulsion progresses, however, a change occurs in cerebral blood flow, dependent on the altered relationship of blood gases and changes in blood pressure. Any change in cerebral blood flow following the convulsion is temporary, as indicated by the return of blood gases to original levels within a short time after the convulsion. There is no similarity between insulin hypoglycæmia and a metrazol convulsion as regards changes in the relationship of dextrose and oxygen. The cerebral hypoxia occurring in the former condition has only a superficial resemblance to the cerebral hypoxia of the latter condition. So far as these data are concerned, changes in mental states following metrazol convulsions and insulin hypoglycæmia cannot be explained on the basis of any common alteration in either cerebral chemistry or cerebral blood flow. (R. M. S.)

Influence of Insulin on Blood.—When insulin leads to a fall of the blood sugar below 50 mg. per hundred cubic centimetres, this is accompanied by a fall in the carbon dioxide tension of the alveolar air. Restoration of the blood sugar level leads to a rise in the carbon dioxide tension (experiments on schizophrenic patients). In deep coma the carbon dioxide tension of the alveolar air at a given level of the blood sugar is higher than at similar levels before coma occurs. The carbon dioxide tension of the arterial blood is lowered during insulin hypoglycæmia and restored to control levels in unanæsthetized dogs on injection of dextrose. General excitement induced by painful stimuli and struggle leads to rise of the blood sugar and lowering of the carbon dioxide tension of the arterial blood in unanæsthetized dogs. Injection of metrazol or epinephrine has effects on the carbon dioxide tension and the sugar of arterial blood similar to those of general excitement. All effects are reversible and are not accompanied by a change in the *p*H of the arterial blood. It is assumed that excitation of the sympathetic nerve centres is responsible for the decrease in carbon dioxide tension of the arterial blood and of the alveolar air.
(R. M. S.)

Paraplegia in Flexion.—The author contributes a valuable discussion of the factors underlying cases of spinal and cerebral paraplegia in flexion. (R. M. S.)

Amyotrophic Lateral Sclerosis.—Hassin concludes that in amyotrophic lateral sclerosis the pathological picture in the pons is the reverse of that in olivopontocerebellar atrophy, in which a different system of ganglion cells is affected. (R. M. S.)

ARCHIVOS ARGENTINOS DE NEUROLOGIA

Vol. 21. Nos. 5–6. November–December 1939.

Estructura y Conexiones del Nucleo Supraóptico del Hombre. (Structure and connections of the supra-optic nucleus in man.) M. Balado and E. Franke. 275.

Alteraciones Neurológicas Consecutivas a Lesiones Traumáticas de la Corteza Cerebral en el Hombre. (Cortical lesions in man following trauma.) S. O. Alcalde. 295.

Hematoma Subdural Crónico. (Chronic subdural hæmatoma.) B. B. Spota, G. H. Dickmann, and A. J. Alurralde. 315.

Epiduritis Supurada. (Suppurative epidural lesions.) R. H. Sirven. 334.

Vol. 22. Nos. 1–2, 3–4. January–April 1940.

Asociación Médica Panamericana. Congreso Julio de 1941, Buenos Aires, Sección Neurologia y Neurocirugia. Temas Propuestos Hasta la Fecha. 5.

Sobre la Dirección de las Corrientes Eléctricas de la Corteza Cerebral. (Action potentials of the cerebral cortex.) M. Balada and L. F. Romero. 7.

Estudio Anátomopatológico de Siete Tumores de Epifisis y uno Yuxtaepifisiario. (Anatomo-pathological study of tumours of the epiphysis and neighbouring structures.) J. M. Prado. 21.

BRAIN

Vol. 63. No. 1. March 1940.

*The Forms of Growth in Gliomas and their Practical Significance. H. J. Scherer. 1.

*Pyramidal Lesion in the Monkey. S. S. Tower. 36.

*The Angioarchitecture of the Gliomata. J. Hardman. 91.

Forms of Growth in Gliomas.—Large sections were made of 120 gliomatous brains. All the gliomas except ependymomas showed very wide infiltration, irrespective of the rate of tumour growth. Only 30 per cent. were relatively circumscribed, while 60 per cent., including all astrocytomas, showed diffuse changes beyond the expected limits of the tumour. The remainder, especially glioblastomas, showed multicentral growth. Brain tissue was often preserved in the infiltrated areas. The methods of spread are described. (D. J. W.)

Pyramidal Lesion in Monkey.—The behaviour of monkeys was observed after section of the medullary pyramids. The lesions were later examined at autopsy and the corticospinal pathways studied histologically. As the basis of the functional changes observed in the animals some aspects of motor function have been reconsidered at very great length. The discussion is modified by the finding of hypotonia after the pyramidal section. (D. J. W.)

Angioarchitecture of Gliomata.—The blood vessels of 25 cerebral gliomas were studied histologically after staining with Pickworth's technique. The vascular formations found are described with reference to malignancy, central necrosis, cyst formation, and the form of tumour growth. (D. J. W.)

L'ENCÉPHALE

Vol. 34 (2). No. 1. June 1939.

Recherches sur 100 Malades Entrés au "Service Spécial des Aliénés Alcoholiques" du Département de la Seine. (Investigations of 100 cases in the special service for alcoholic psychoses.) J Dublineau and H. Duchêne. 275.

Combinaison de l'Amyotrophie de Charcot-Marie-Tooth et de la Maladie de Friedreich, chez Plusieurs Membres d'une Même Famille. (Combination of Charcot-Marie-Tooth amyotrophy and Friedreich's ataxia in several members of the same family.) L. van Bogaert and M. Moreau. 312.

JOURNAL BELGE DE NEUROLOGIE ET DE PSYCHIATRIE

Vol. 39. No. 12. December 1939.

La Projection des Noyaux Antérieurs du Thalamus sur L'Écorce Interhémisphérique. (The projection of the anterior nucleus of the thalamus in the cortex.) J. Stoffels. 783.

Vol. 40. No. 1. January 1940.

Étude Anatomo-Clinique d'un Cas de Chorée de Sydenham. (Clinico-anatomical study of a case of Sydenham's chorea.) M.-T. Callewaert. 5.

Ophtalmoplégie Bilatérale par Propagation Intracrânienne d'une Tumeur du Sinus Maxillaire Droit. (Bilateral ophthalmoplegia by intracranial extension of a tumour of the right maxillary sinus.) M. André. 21.

Polyradiculo-Névrite Récidivante, du Type Guillain-Barré, à Forme Pseudo-tabétique. (Polyneuroradiculitis of the Guillain-Barré type.) M. André (Brussels). 28.

Ataxie Cérébelleuse avec Aréflexie Généralisée Survenue Progressivement dans le Décours d'une Coqueluche. (Cerebellar ataxia with generalized areflexia following whooping-cough.) E. Kokken. 39.

Vol. 40. No. 2. February 1940.

*Étude Neuropathologique de la Maladie de Niemann-Pick (Spléno-Hépatomégalie Lipidienne.) (Neuropathological study of a case of Niemann-Pick's disease.) R.-A. Ley. 57.

Sur une Forme Chronique à Évolution Fatale de la Dermatomyosite avec Sclérodermie. (On a chronic form with fatal termination of a case of dermatomyositis with sclerodermia.) Mme. Rademecker. 83.

Niemann-Pick's Disease.—An exhaustive study of the above condition with many very excellent illustrations. (E. A. C.)

Vol. 40. No. 3. March 1940.

Trois Cas de Kleptomanie. (Three cases of kleptomania.) H. Grelinger. 105.

Paralysie de Lissauer. (Lissauer's paralysis.) P. Divry. 118.

*Syndrome de Parinaud. Étude Anatomique. (Parinaud's syndrome. Anatomical study.) P. Van Gehuchten. 126.

Un Cas de Tumeur Perlée de la Région Épiphysaire. ("Perly" tumour in the region of the epiphysis.) P. Van Gehuchten, J. Morelle, and A. Dereymaker. 134.

Cardiazol et Lésions Cérébrales. (Cardiazol and cerebral lesions.) M. Leroy. 140.

Spasmes Oppositionnistes chez un Paralytique Général Malarisé. (Oppositonic spasms in a case of G.P.I.) J. Ley and J. Titeca. 153.

Maladie de Kussmaul-Maier et Sclérose Diffuse. (Kussmaul-Maier's syndrome in diffuse sclerosis.) J. Balo. 160.

Parinaud's Syndrome.—In the case of an old man with sudden onset of difficulty in looking upwards voluntarily, with less affected automatic reflexes of upward movement and with preservation of pupillary reflexes, the author found a lesion of the posterior commissure and in the immediate neighbourhood of the nucleus of Darkschewitsch. (E. A. C.)

JOURNAL OF CLINICAL INVESTIGATION

Vol. 19. No. 2. March 1940.

Studies on Neoplasms with the Aid of Radioactive Phosphorus. I. The Total Phosphorus Metabolism of Normal and Leukemic Mice. J. H. Lawrence, L. W. Tuttle, K. G. Scott, and C. L. Connor. 267.

A Comparison of Procedures for Increasing Blood Flow to Limbs using an Improved Optical Plethysmograph. G. M. Wright and K. Phelps. 273.

The Determination of the Glomerular Filtration by the Endogenous Creatinine Clearance. K. Steinitz and H. Türkand. 285.

Studies of the Conditions of Glucose Excretion in Man. K. Steinitz. 299.

Antibody Formation in Cases of Lobar Pneumonia Treated with Sulfapyridine. Y. Kneeland and B. Mulliken. 307.

Electrophoretic Analysis of Plasma and Urinary Proteins. J. A. Luetscher. 313.

The Effect of Unilateral Spontaneous Pneumothorax on the Circulation in Man. H. J. Stewart and R. L. Bailey. 321.

Calcium and Phosphorus Metabolism in Osteomalacia. IX. Metabolic Behaviour of Infants Fed on Breast Milk from Mothers showing Various States of Vitamin D Nutrition. S. H. Liu, H. I. Chu, C. C. Su, F. T. Yu, and H. C. Chao. 327.

Calcium and Phosphorus Metabolism in Osteomalacia. X. Further Studies on Vitamin D Action: Early Signs of Depletion and Effect of Minimal Doses. H. I. Chu, S. H. Liu, F. T. Yu, H. C. Hsu, T. Y. Cheng, and H. C. Chao. 349.

Observations on the Plasma Prothrombin and the Effects of Vitamin K in Patients with Liver or Biliary Tract Disease. F. J. Pohle and J. K. Stewart. 365.

Observations on the Serum Cholesterol in Acute Infection as Recorded during and after Pneumonia. A. Steiner and K. B. Turner. 373.

Four Recent Influenza Epidemics: An Experimental Study. F. L. Horsfall, R. G. Hahn, and E. R. Rickard. 379.

Studies of Rheumatic Disease. III. Familial Association and Aggregation in Rheumatic Disease. R. L. Gauld and F. E. M. Read. 393.

*Urinary Excretion of Thiamin in Clinical Cases and the Value of Such Analyses in the Diagnosis of Thiamin Deficiency. W. D. Robinson, D. Melnick, and H. Field. 399.

The Glycine Tolerance Test in Sprue and Pernicious Anæmia. L. A. Erf and C. P. Rhoads. 409.

A Study of Sulfur Metabolism and the Effect of Sulfur Administration in Chronic Arthritis. R. H. Freyberg, W. D. Block, and M. F. Fromer. 423.

Urinary Excretion of Thiamin.—It is shown that urinary thiamin excretion is a fairly reliable index to the adequacy of the preceding diet in respect to this vitamin. Low thiamin excretions were obtained from patients with "alcoholic beri-beri," while diabetic and hyperthyroid patients had normal urinary thiamin values. (J. N. C.)

Vol. 19. No. 3. May 1940.

Ballistocardiogram. II. Normal Standards, Abnormalities commonly found in Diseases of the Heart and Circulation, and their Significance. I. Starr and H. A. Schroeder. 437.

Increased Urobilinogen Excretion and Acute Hæmolytic Anæmia in Patients treated with Sulfapyridine. L. A. Erf and C. M. MacLeod. 451.

Distribution of Ascorbic Acid in the Blood and its Significance. A. M. Butler and M. Cushman. 459.

Factors that Influence the Passage of Ascorbic Acid from Serum to Cells in Human Blood. M. Heinemann and P. M. Hald. 469.

Renal Blood Flow in Women with Hypertension and Renal Impairment. L. C. Chesley and E. R. Chesley. 475.

*Correlation between the Concentration of Bisulphite Binding Substances in the Blood and the Urinary Thiamin Excretion. W. D. Robinson, D. Melnick, and H. Field. 483.

The Influence of Vitamin A upon Urea Clearance in the Human Subject. R. C. Herrin and H. J. Nicholes. 489.

Blood Changes induced by Venesection in Women with Toxæmia of Late Pregnancy. F. W. Oberst and E. D. Plass. 493.

*The Effect of Benzedrine (β-Phenylisopropylamine

Sulphate) and Paradrine (*p*-Hydroxy-*d*-Methyl-Phenylethylamine Hydrobromide) on the Circulation, Metabolism, and Respiration in Normal Man. M. D. Altschule and A. Iglauer. 497.
The Effect of Paradrine on the Venous System. A. Iglauer and M. D. Altschule. 503.
Observations on the Blood Iodine. I. The Blood Iodine in Health, in Thyroid and Cardiorenal Disease, and in Leukemia. K. B. Turner, A. Delamater, and W. D. Province. 515.
Renal Function in Patients with Gout. F. S. Coombs, L. J. Pecora, E. Thorogood, W. V. Consolazio and J. H. Talbot. 525.
The Relation of Specific Gravity to Composition and Total Solids in Normal Human Urine. J. W. Price, M. Miller, and J. M. Hayman. 537.

Effect of Benzedrine and Paradrine on Circulation, Metabolism, and Respiration.—These two papers show the effect of benzedrine and paradrine on respiration and circulation. Both raise systolic and diastolic blood pressure with no alteration in cardiac output or in respiratory dynamics. Paradrine produces as well a generalized increase of venous pressure, and it is suggested that this increase is due to active constriction of the veins. (J. N. C.)

Correlation between Bisulphite Binding and Urinary Thiamin.—There is shown to be no correlation between the urinary thiamin and the blood bisulphite binding substances and also that the determination of the B. B. S. lacks sensitivity and specificity for determining thiamin deficiency. (J. N. C.)

JOURNAL OF COMPARATIVE NEUROLOGY

Vol. 72. No. 1. February 1940.

Certain Basal Telencephalic Centers in the Cat. C. A. Fox. 1.
The Cerebellum of the Rabbit. A Topographical Atlas of the Folia as revealed in Transverse Sections. A. Brodal. 63.
Differentiation of the Bulbar Motor Nuclei and the Coincident Development of Associated Root Fibers in the Rabbit. D. L. Kimmel. 83.
The Telencaphalic Zonal System of the Teleost Corydora Paliatus. R. N. Miller. 149.
The Efferent Fibers of the Thalamus of Macaccus Rhesus. II. The Anterior Nuclei, Medial Nuclei, Pulvinar, and Additional Studies on the Ventral Nuclei. R. L. Crouch. 177.
The Nuclear Masses in the Cervical Spinal Cord of Macacca Mulatta. A. F. Reed. 187.

Vol. 72. No. 2. April 1940.

Studies on the Diencephalon of the Virginia Opossum. Part II. The Fiber Connections in Normal and Experimental Material. D. Bodian. 207.
The Cerebral Cortex in some Tinamidæ. E. H. Craigie. 299.
The Hypothalamus of the Coney, Hyrax Syrica. J. S. Jessup and W. M. Shanklin. 329.
The Innervation of the Biliary System. W. F. Alexander. 357.
The Structural Organization of the Inferior Mesenteric Ganglia. A. Kuntz. 371.
An Analysis of the Problem of Emergent Fibers in Posterior Spinal Roots, dealing with the Rate of Growth of Extraneous Fibers into the Roots after Ganglionectomy. W. H. L. Westbrook. 383.
Morphology of the Cerebellar Nuclei in the Rabbit and Cat. R. S. Snider. 399.
A Comparative Fiber and Numerical Analysis of the Pyramidal Tract. A. M. Lassek and G. L. Rasmussen. 417.

Vol. 72. No. 3. June 1940.

Cortical Lamination in the Monotremata. A. A. Abbie. 429.
The Excitable Cortex in Perameles, Sarcophilus, Dasyurus, Trichosurus, and Wallabia (Macropus). A. A. Abbie. 469.
The Hypoglossal Complex of Vertebrates. J. W. Barnard. 489.
Comparison of the Changes caused by Fatigue and by Ageing in the Cerebral Cortex of Mice. W. Andrew and N. V. Andrew. 525.
Supra- and Post-Optic Commissures in the Brain of the Rat. Y. Tsang. 535.
Partial Agenesis of the Cerebellum in Dogs. R. S. Dow. 569.
A Quantitative and Experimental Study of the Cervical Sympathetic Trunk. J. O. Foley and F. S. Dubois. 587.
The Respiratory Center and its Descending Pathways.

JOURNAL OF MENTAL SCIENCE

Vol. 86. No. 362. May 1940.

Morgagni's Syndrome: A Clinical and Pathologica Study. R. E. Hemphill and E. Stengel. 341.
The Contribution of the Rorschach Method to Wartime Psychological Problems. M. R. Harrower-Erichson. 366.
Prognosis in Schizophrenia. D. Blair. 378.
Adaptiveness and Equilibrium. W. R. Ashby. 478.
Has Fear any Therapeutic Significance in Convulsive Therapy? L. C. Cook. 484.
Some Observations on the Psychological Aspects of Cardiazol Therapy. R. Good. 491.
The Influence of Cardiazol on Chronic Schizophrenia. A. J. Bain. 502.
*The Relationship between Disturbance of Liver Function and Mental Disease. P. Berkenau. 514.
Prolonged Narcosis with Paraldehyde and Dial. M. B. Brody. 526.
A Note on the Use of the 1937 Revision of the Stanford Binet Vocabulary List in Mental Hospital Patients. M. B. Brody. 532.
Ascorbic Acid in Patients suffering from Psychoses of the Senium. D. G. Remp, J. B. Ziegler, and D. E. Cameron. 534.

Liver Function and Mental Disease.—The liver function of 32 patients with mental disease was tested by means of the oral hippuric acid synthesis test, the Takata reaction and other tests. Hippuric acid synthesis was found to be deficient in all the 15 cases showing catatonic features and normal in the remainder. The Takata reaction was positive in 10 of the 14 cases in the catatonic group, and negative in the non-catatonic group, except for 2 chronic alcoholics. The author speculates as to the relationship between the liver impairment and the mental state. (B. McA.)

JOURNAL OF NERVOUS AND MENTAL DISEASE

Vol. 91. No. 2. February 1940.

Poetry in Schizophrenia and Other Psychoses. L. Kerschbaumer. 141.
*A Comparison of the Medical and Surgical Treatment in Hypertension with Special Reference to the Importance of Psychic Factors in Evaluating the Results, with a Report of Ninety-Two Cases treated Medically. S. K. Robinson. 157.
Insulin Shock Therapy in Korsakoff's Psychosis. P. C. Talkington and T. H. Cheavens. 175.
Neurodermatitis-Pain-Shock-Distilled Water. A. N Foxe. 184.
A Simple Version of Aphasia. L. B. Alford. 190.

Comparison of Medical and Surgical Treatment in Hypertension.—Psychotherapy is considered the most important factor in the treatment of hypertension. (W. M. H.)

Vol. 91. No. 3. March 1940.

*The Goodenough Test (Drawing of a Man) in Chronic Encephalitis in Children. L. Bender. 277.
Suicide among Hospitalized Drug Addicts. M. J. Pescor and P. A. Surgeon. 287.
The Great Delusion. J. Favill. 306.
Retrospective Study of a Case involving Homicide. T. K. Rathmell and K. M. Corrin. 316.
Shall We Differentiate between Schizophrenia and Dementia Præcox? L. Wallingford Darrah. 323.
Problems of Shock Treatment in Schizophrenics. F. Kant, P. L. Phillips, and R. M. Stolzheise. 329.

Goodenough Test in Chronic Encephalitis.—Failure in this test is related to perceptual difficulties in relation to the body. With disturbance of motility the body image is poorly integrated as shown by the drawing of the human form. (W. M. H.)

Vol. 91. No. 4. April 1940.

Grasping: "Forced" and "Non-Forced." I. Bieber. 417.
Electrocardiographic Studies after Treatment with Insulin and Metrazol Shock. R. Sonethal and A. A. Low. 423.
Study of the Hemato-Encephalic Barrier by the Bromide Method, before and after Insulin Therapy. M. M. Kessler. 428.
Pneumothorax in Treatment of Pulmonary Tuberculosis in Psychotic Patients. E. F. Dombrowski, F. S. Rankin, and H. H. Goldstein. 449.
Myoclonus Epilepsy with Primary Optic Atrophy. M. P. Rosenblum and M. Herman. 456.
Behaviour Problem in Children from the Homes of Followers of Father Divine. L. Bender and M. A. Spalding. 460.

JOURNAL OF NEUROPATHOLOGY AND PSYCHIATRY, LENINGRAD

Vol. 8. No. 11. 1939.

The Treatment of Schizophrenia with Sulphozin (on the Children). V. J. Dejanov. 3.
Histopathology of the Hepatolenticular Degeneration. N. V. Konovalov. 14.
To the Morbid Anatomy and Etiology of the Amiotrophic Lateral Sclerosis. G. G. Sokoljansky. 35.
Pathophysiology of the Hallucinations and Other Disorders of the Perception in the Light of the Hypnotical Experiment. V. I. Kouravitsky. 50.
Inversive Forms of Cerebral Paralyses in the Subcortical Pathology. L. B. Litvak. 53.
Lumbar Puncture in the Closed Traumas of the Skull as Diagnostic and Therapeutic Method. A. B. Rogover. 67.

Vol. 8. No. 12. 1939.

Cytology of the Liquor. D. A. Shamburova and L. L. Sinegubko. 11.
Connection of the Peripheral Sympathetic System with the Central Nervous System through the Hypophysis. B. M. Sokolov. 30.
Administration of Nicotinic Acid in Pellagra. M. J. Serejsky. 39.
The Pathogenesis of Paroxysmal Myoplegia. L. A. Kvint. 44.
On the Index of Rational Utilization of the Bed Fund in the Psychiatric Hospital. I. A. Ossovsky. 50.
Abstinential Shock and Korsakov's Psychosis in the Heroinisme. V. A. Gorovoi-Shaltan. 59.
The Clinic of Arsenical Polyneuritis. V. P. Pervushin and G. S. Rusakov. 67.
Comparative Physiology of the Plasticity of the Nervous System. A. I. Karamian. 73.
On the Peculiarities of the Psychic Modifications in Myoclonus-Epilepsy. V. K. Skobnikova. 80.
Results of the Treatment of Narcolepsy with Ephedrin in Combination with Luminal. M. I. Sandomirsky. 87.
On the Investigation of the Sensitiveness by the Compressed Air Method. D. I. Panchenko. 93.
Cerebello-Pyramidal Syndrom in a Brother and a Sister. G. H. Bykhovskaya and I. I. Shtilbans. 96.
Zone of the Trauma of the Brain and Encephalography. I. L. Benkovitch. 100.

JOURNAL OF NEUROPHYSIOLOGY

Vol. 3. No. 1. January 1940.

*Spinal Cord Regeneration in Rat. O. Sugar and R. W. Gerard. 1.
*Paleocerebellar Inhibition of Vasomotor and Respiratory Carotid Sinus Reflexes. G. Moruzzi. 20.
Brain Potential Changes in Man during Cyclopropane Anæsthesia. M. A. Rubin and H. Freeman. 33.
*Conditioned Vestibular Reactions. H. Löwenbach and W. H. Gantt. 43.
*Modification of the Cortical Frequency Spectrum by Changes in Carbon Dioxide, Blood Sugar, and Oxygen. F. A. Gibbs, D. Williams, and E. L. Gibbs. 49.
Ocular Rotation in Anæsthesia and under the Influence of Supranuclear Centres. E. A. Spregel and D. A. Collins. 59.
*Effect of Various Cortical Lesions on Development of Placing and Hopping Reactions in Rats. C. McC. Brooks and M. E. Peck. 66.
*Activity of Isocortex and Hippocampus. Electrical Studies with Micro-Electrodes. B. Renshaw, A. Forbes, and B. R. Morison. 74.

Spinal Cord Regeneration.—The spinal cord of rats was sectioned between T5 and T13 and a gap of 2–3 mm. ensued by tension maintained on the tail. After four weeks of spinal performance sensory and motor recovery was shown by voluntary climbing, walking, placing and seeking based on proprioception. Stimulation of the brain stem at sacrifice produced hind leg movements. New axones from cord tracts and spinal roots were found to bridge the gap. Their growth was aided by implant of degenerating sciatic nerve. (W. M. H.)

Paleocerebellar Inhibition of Carotid Sinus Reflexes.—Weak faradic stimulation of the vermian cortex of the anterior cerebellum inhibits carotid sinus vasopressor and respiratory reflexes produced by carotid occlusion, and reflexes, chiefly respiratory, induced by intracarotid KCN. These effects are due to inhibition of bulbopontine centres. (W. M. H.)

Conditioned Vestibular Reactions.—In dogs vestibular reflexes as elicited by galvanic current were readily produced as conditioned responses to an auditory stimulus. Prolonged deep and peculiar motor phenomena developed in one of four dogs. (W. M. H.)

Modification of Cortical Frequency Spectrum.—The Grass frequency analyser showed that with increase in CO_2 of internal jugular blood there is a shift of cortical frequencies toward the fast side. Oxygen and glucose may be varied in wide limits with little change in the frequency spectrum. When O_2 or glucose fall critically there is sudden shift to the slow side ; with very high glucose a shift to the fast. (W. M. H.)

Cortical Lesions and Placing and Hopping Reactions.—The control of hopping and placing reactions is localized to the sensorimotor cortex and on removal of the area in the rat of 1–5 days, which corresponds to the sensorimotor cortex of the adult, no other part of the cortex or subcortical structure can assume this control. In the area there is some subdivision of function. (W. M. H.)

Isocortex and Hippocampus Activity.—Micro-electrode techniques for study of electrical changes in the nervous system are described. In the isocortex and hippocampus the activity of only a small volume of adjacent tissue is recorded. Contrasted with the slow waves from various positions in the hippocampus are rapid deflections of 1 m.sec. in duration, negative in their predominant phase, recorded only in or near the strata containing the pyramidal cell bodies of Ammons' horns. Responses to stimulation of afferent fibre are taken to represent activity of perikarya of the pyramidal cells. (W. M. H.)

Vol. 3. No. 2. March 1940.

*Facilitation and Difficilitation effected by Nerve Impulses in Peripheral Fibers. J. Erlanger and E. A. Blair. 107.
A Human Cortical Area producing Repetitive Phenomena when Stimulated. R. M. Brickner. 128.
Effects of Eserine, Acetylcholine and Atropine on the Electrocorticogram. F. R. Miller, G. W. Stavraky, and G. A. Woonton. 131.
*Cord Potentials in Spinal Shock—Single Volleys. W. B. Stewart, J. Hughes, and G. P. McGough. 139.
*Cord Potentials in Spinal Shock—Multiple Stimuli. J. Hughes, G. P. McCouch, and W. B. Stewart. 146.
Cord Potentials in Spinal Shock—Crossed Effects in Monkey—*Macacca Mulatta*. G. P. McCouch, W. B. Stewart, and J. Hughes. 151.
*An Attempt to Produce Sleep by Diencephalic Stimulation. F. Harrison. 156.
Relayed Impulses in Ascending Branches of Dorsal Root Fibers. J. B. Hursh. 166.
*Observations upon Diaphragmatic Sensation. J. C. Hinsey and R. A. Phillips. 175.
*The Phasic Response to Cortical Stimulation. C. G. Smith, F. A. Mettler, and E. A. Culler. 182.

Facilitation Affected by Nerve Impulses.—The facilitating action of spikes at a block produced by anodal polarization increases with their number and frequency. In a tetanus if a spike passes the block all the succeeding spikes will pass ; but when conduction is produced by facilitation a momentary interruption of the tetanus will interrupt conduction. In its early stages this difficilitation represents the subnormal phase of the excitability cycle beyond a block when tetanic stimulation is interrupted. These features of facilitation and difficilitation may have analogies in actual synapses. (W. M. H.)

Cord Potentials in Spinal Shock—Single Volleys.—After spinal transection the threshold for cord potential and ipsilateral flexor reflex are in the cat and dog equal to that of afferent nerve; in the monkey reflex threshold reaches the level of nerve threshold only after 12 days. In the cat and dog spinal shock is at the internuncial level; in the monkey as well as internuncial depression there is deep and prolonged shock to the motor neurones. **Multiple Stimuli.** In the spinal monkey inhibition of the internuncial response to the second of two volleys depends on the positive wave in the preceding cord potential. With repetitive stimulation there is little increase in positivity. Such behaviour is in contrast to that of peripheral nerve and suggests that the sources of negativity and positivity are different. (W. M. H.)

Diencephalic Stimulation and Sleep.—Somnolence is produced in cats by destructive electric currents to the lateral hypothalamic area. Catalepsy develops with lesions of the medial and caudal parts of the hypothalamic area. Stimulation of these structures fails to give somnolence. (W. M. H.)

Diaphragmatic Sensation.—In man pain may be referred to a completely anæsthetized area of skin in the shoulder tip when the central diaphragmatic peritoneum is stimulated. In the cat and dog nociceptive sensibility produced by like stimulation is independent of afferent fibres of the vagus, intercostal nerves, and efferent sympathetic fibres. Viscero-cutaneous reflexes are therefore not essential for nociceptive sensation with this type of stimulation. (W. M. H.)

Phasic Response to Cortical Stimulation.—Phasic responses to cortical stimulation depend on proprioceptive impulses passing from dorsal roots through the ventral spino-cerebellar tract. (W. M. H.)

JOURNAL OF PHYSIOLOGY

Vol. 97. No. 4. February 1940.

The Formation of Urine in the Amphibian and Mammalian Kidney. P. Ellinger. 433.
*The Action of Some Amines Related to Adrenaline. Cyclohexylalkylamines. J. A. Gunn and M. R. Gurd. 453.
*Electric Interaction between Two Adjacent Nerve Fibres. B. Katz and O. H. Schmitt. 471.
The Lipotropic Action of Methionine. C. H. Best and J. H. Ridout. 489.
The Action of Embryonic Extracts of the Sex Organs. H. L. Meyerhof and A. Zironi. 495.
The Absorption of Monosaccharides from the Distal Small Intestine of Anæsthetized Cats. J. N. Davidson and R. C. Garry. 509.
Prolongation of Pregnancy in the Hypophysectomized Rabbit by Progesterone and Œstrogens. J. M. Robson. 517.
*Respiratory Reflexes in the Fowl. J. D. P. Graham. 525.

Action of Amines Related to Adrenaline.—The effect of reduction of the benzine ring in a series of amines related to adrenaline is to produce little if any qualitative change in physiological activity. With both cyclohexyl and phenyl compounds central stimulant properties increase in the order methylamine < ethylamine < isopropylamine. Cyclohexenyliso propylamine is exceptionally strong as a cerebral stimulant. It is also more toxic than the corresponding phenyl and cyclohexyl compounds. (W. M. H.)

Electric Interaction between Adjacent Nerve Fibres.—In the limb nerve of the crab excitability changes are shown in one fibre during the passage of an impulse in the adjacent fibre. Alterations in conduction rate are explained by simple summation of the local currents of the two fibres. (W. M. H.)

Respiratory Reflexes in Fowl. The Hering-Breuer reflex is present in a modified form in the fowl. Negative ventilation has no effect on respiration. Distension of the lungs and air sacs is a stimulus for the first part of the reflex whereby inspiration is inhibited. Expiration begins as a passive movement and is promoted by the passage of air up the trachea—an effect which is abolished by high vagal section or cocainization of the trachea. (W. M. H.)

Vol. 98. No. 1. March 1940.

Glycogen and Calcification. G. E. Glock. 1.
*The Effect of Temperature on the Mechanical Response and the Viscosity and Oxygen Consumption of Unstriated Muscle. M. S. Rao and I. Singh. 12.
*Partial Excitation and Variable Conduction in the Squid Giant Axon. F. O. Schmitt and O. H. Schmitt. 26.
*Correlation of Local Excitability with Local Physiological Response in the Giant Axon of the Squid (*Loligo*). R. J. Pumphrey, O. H. Schmitt, and J. Z. Young. 47.
The Composition of Alveolar Air. I. F. S. Mackay. 73.
Effect of Gravity on the Blood Pressure of the Cat. O. G. Edholm. 79.
The Renal Excretion of Inulin and Creatinine by the Anæsthetized Dog and the Pump-Lung-Kidney Preparation. J. A. Shannon and F. R. Winton. 97.
Capillary Permeability and Œdema in the Perfused Frog. J. F. Danielli. 109.
*The Inactivation of Adrenaline by Phenolases. H. Blascho and H. Schlossmann. 130.

Temperature and Mechanical Response, Viscosity and Oxygen Consumption of Muscle.—In Mytilus muscle decrease in temperature and tonic contractions diminish the rate of rise of tension during A.C. stimulation. While most tonic contractions increase the O_2 uptake it falls with shortening produced by Na and NH_4 ions. Isotonic NaCl causes frog muscle to lose weight ; Ca antagonizes this action. (W. M. H.)

Excitation and Conduction in Giant Axon.—The advantages of the giant axon (about 0·5 mm. in diameter) of the squid are exploited in a study of temporal and spatial distributions of potential with varied intensity of shock. Local partial excitation is shown in the depressed fibre with near threshold stimuli. The response is found to increment or decrement only slowly over a considerable length of nerve. No changes in birefringence occur in the axis cylinder. (W. M. H.)

Excitability and Physiological Response in Giant Axon.—In single nerve fibres of the squid variations in excitability may be correlated with the local potentials developed by conditioning stimuli. Excitation arises from the electrical summation of components of local action currents and the applied stimuli. Excitability curves for single squid fibres resemble those found for bundles of frog sciatic fibres. A refractory period of local response is found *circa* 1 m.sec. after a just sub-threshold conditioning stimulus. (W. M. H.)

Inactivation of Adrenaline by Phenolases.—When inactivated by polyphenol oxidase and by the cytochrome system adrenaline takes up rapidly 2 atoms O_2 per mol. and forms adrenochrome. A further slow uptake of O_2 occurs independent of the enzyme and the red colour changes to brown. Inactivation of adrenaline by peroxidase cannot be measured manometrically. (W. M. H.)

Vol. 98. No. 2. May 1940.

*The Permeability of the Blood-Aqueous Humour Barrier to Potassium, Sodium, and Chloride in the Surviving Eye. H. Davson and J. P. Quilliam. 141.

The Effect of the Interaction of Ions, Drugs, and Electrical Stimulation as indicated by the Contraction of Mammalian Unstriated Muscle. I. Singh. 155.

*Discharges from the Sensory Organs of the Cat's Vibrissæ and the Modification in Their Activity by Ions. O. Fitzgerald. 163.

Transmission of Light by the Eye Media. K. J. W. Craik. 179.

The Effect of Mono-Iodoacetic Acid on the Absorption of Water from Glucose Solutions in the Subarachnoid Space. T. H. B. Bedford. 185.

The Part Played by the Renal Nerves in the Production of Water Diuresis in the Hypophysectomized and Decerebrate Dog. L. E. Bayliss and A. Brown. 190.

The Time Course of the Oxygen Consumption of Stimulated Frog's Muscle. D. K. Hill. 207.

*Determination of the Metabolic Rate of Alcohol. M. G. Eggleton. 228.

*Some Factors affecting the Metabolic Rate of Alcohol. M. G. Eggleton. 239.

The Results of Adrenalectomy in the Pregnant Albino Rat. T. McKeown and W. R. Spurrell. 255.

Permeability of Blood-Aqueous Humour in Eye.—The membrane separating the eye fluids from blood is not specifically impermeable to cations, nor does it show undirectional permeability. The membrane does not secrete K, and probably not Na or Cl. (W. M. H.)

Discharge from Sensory Organs of Cat's Vibrissæ.—The nerve endings stimulated by movement of the vibrissæ are slowly adapting. The duration of the silent period following stimulation in a nerve fibre giving a spontaneous discharge is related to the total number of impulses discharged. K in small amounts leads to spontaneous discharges and an increased initial discharge. K is not likely an agent for rapid adaption of endings. (W. M. H.)

Metabolic Rate of Alcohol (2 papers).—(*a*) Following intravenous alcohol equilibrium between content of muscle and plasma occurs in 1–1¼ hours. Most tissues contain 70–80 per cent., and fat 10–20 per cent. the concentration of alcohol in the plasma. The factor *r* (concentration of alcohol in whole body expressed as a fraction of that in the plasma) is constant in one animal but varies among animals. (*b*) The metabolic rate of alcohol depends on the concentration in the body. The rate per unit liver weight in animals previously fed with alcohol is significantly smaller than in normal animals. The rate is increased by addition of alanine to the body. (W. M. H.)

PHYSIOLOGICAL REVIEWS

Vol. 20. No. 2. April 1940.

Experimental Hypertension. A. Blalock. 159.

Plasma Proteins: Their Source, Production, and Utilization. S. C. Madden and G. H. Whipple. 194.

The Study of Intermediary Metabolism of Animals with the Aid of Isotopes. R. Schoenheimer and D. Rittenberg. 218.

Relation of Nicotinic Acid to Pellagra. C. A. Elvehjem. 249.

The Physiology of Articular Structures. W. Bauer, M. W. Ropes, and H. Waine. 272.

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Vol. 14. No. 2. April 1940.

Psychopathic Personality among the Mentally Defective. E. J. Humphreys. 231.
The Problem of Treating Psychopaths. L. P. O'Donnell. 248.
An Approach to the Problem of Psychopathic Personality. R. A. Savitt. 255.
The Neuropathology of Benzedrine Poisoning. P. G. Schube and N. Raskin. 264.
A Simple Experimental Device for the Prediction of Outcome of Insulin Treatment in Schizophrenia. Z. Piotrowski. 267.
Therapeutic Considerations in Psychoses of Old Age. G. F. Etling. 274.
Ideas of Neglect and Hoarding in the Senile Psychoses. M. D. Riemer. 285.
The Psychiatric Examination of the Criminotic Individual. A. N. Foxe. 289.
Determining the Prognosis in the Involutional Psychoses. J. A. Brussel. 301.
The Injection Treatment of Varicose Veins in a State Hospital. M. A. Yost. 307.
Testosterone in Psychotic Male Homosexuals. H. S. Barahal. 319.
The Premarital Interview. S. W. Wortis. 331.
Personality Factors in Alcoholic Psychoses. P. H. Hoch. 338.
Therapeutic Problems in the Alcoholic Psychoses. C. E. Howard and H. M. Hurdum. 347.
A Brief Review of the Research and Teaching Functions of the New York State Psychiatric Institute and Hospital for the Ten-Year Period 1930–1940. N. D. C. Lewis. 360.
Relative Effects of Phenobarbital and Sodium Bromide as Anticonvulsants in Epileptic Psychoses. R. W. Southerland. 382.
Metrazol Therapy in the Face of Severe Physical Disorders. G. W. Robinson and P. Shelton. 388.
The Force required to Crush Vertebræ: Its Probable Mechanical Relation to the Postmetrazol Fracture. W. Furst. 397.
Alcoholism: Its Frequency, Etiology, and Treatment. W. A. Strong. 403.
The Involutional Psychoses. M. F. Brew and E. Davidoff. 412.

REVUE NEUROLOGIQUE

Vol. 72. No. 4. 1939–1940.

Congrès Neurologique International (Copenhague, 21–25 Août, 1939). (International Neurological Congress at Copenhagen, August, 1939.)

RIVISTA DI NEUROLOGIA (NAPOLI)

Vol. 13. No. 1. February 1940.

*La Nevralgia del Glossofaringeo e le Nevralgie Auricolo-Facciali. (Glossopharyngeal and auriculofacial neuralgia.) C. Pero. 1.
*Su due Casi di Neurofibromatosi di Recklinghausen. (Two cases of Recklinghausen's neurofibromatosis.) P. Giliberti. 27.
*Ulteriori Dati sulla Iodoterapia Endovenosa ed Endodurale. (End results in intravenous and intradural iodine therapy.) A. Rubino and D. Amico. 49.
*La Reazione di Donaggio nell'Elettroshockterapia. (Donaggio's reaction in electro-shock therapy.) A. de Falco. 68.

Glossopharyngeal Neuralgia.—After dealing with the records of glossopharyngeal neuralgia in the literature the author describes a case in which the pain was definitely localized to the lateral wall of the pharynx, the tonsil, the arch of the palate, and the ear, and radiated to the internal surface of the forearm and arm in the distribution of C8–D1. The author explains the mechanism of this limited radiation of the pain by the anastomosis between fibres from the superior cervical ganglion and those from the petrosal ganglion of the glosso-pharyngeal. Similarly, artificial anæsthesias and neuralgias which do not correspond to strict nerve distribution are to be explained by the presence of pain fibres in the carotid plexus which are distributed along the vessels rather than along the nerve trunks. (R. G. G.)

Recklinghausen's Neurofibromatosis.—A full description of the clinical features of two cases and histopathological findings in the tumours are given. The tendency to malignant changes in the tumours is discussed and the author is inclined to suggest that the nervous elements in these may actually take on malignant characteristics. (R. G. G.)

Intravenous Iodine Therapy.—Fifteen cases are described of inflammatory affections of the nervous system (especially leptomeningitis) which were treated by intrathecal along with intravenous iodine. The authors are much impressed by the efficacy of this form of treatment. (R. G. G.)

Donaggio's Reaction in Electro-Shock Therapy.—The reaction is examined in seven cases of schizophrenia treated by electro-shock therapy and the positive findings in six of the cases indicates, according to the author, that this treatment determines an organic modification and disturbance of equilibrium in the nervous system. (R. G. G.)

RIVISTA DI PATOLOGIA NERVOSA E MENTALE

Vol. 55. No. 1. January–February 1940.

*Poliradiculonevrite con Dissociazione Albumino-Citologica (Sindrome di Guillain-Barré-Strohl) con Risentimento Diencefalico. (Polyradiculo-neuritis with cell protein dissociation.) A. Grassi. 1.

*Sulle Distrofie Ossee Croniche con Particolare Riguardo all'Osterporosi Circoscritta del Cranio (Malattia di Schüller). (Chronic dystrophy of bone, particularly localized osteoporosis of the skull.) A. Campana. 64.
*Orientamenti Clinici e Nosografici dopo un Anno di Terapia Insulinica e Cardiazolica in Malati di Mente nella R. Clinica di San Salvi. (Conclusions after a year of insulin and cardiazol therapy in mental patients.) C. E. Roberti. 78.
*Sindrome Neurastenica Constituzionale con Alterazioni Mesodiencefalo - Spinale. (Constitutional neurasthenia and alterations in midbrain and spinal cord.) G. Gomarito. 109.
Idrocefalo da Disturbi Circolatori del Liquor. (Hydrocephalus due to disturbance of the circulation of the C.S.F.) W. Tönnis. 129.
*Lesioni Parenchimatose del Cervelletto da Carcinoma Uterino (Gliosi Carcinotossica?) (Parenchymatous lesions of the cerebellum in carcinoma of the uterus.) D. Alessi. 148.
*Epilessia Sperimentale e Glandole Endocrine. (Experimental epilepsy and the endocrine system.) V. Longo. 175.
Richerche sul Valore delle Manovre di Tobey-Queckenstedt e di Elsberg-Hare per la Semeiotica Manometrica del Liquor. (The value of the Tobey-Queckenstedt and of the Elsberg-Hare tests in determination of C.S.F. pressure.) G. Fasanaro. 195.

Polyradiculo-Neuritis with Cell Protein Dissociation.—The author has reviewed the literature on the subject of the radiculo-neuritis of Guillain-Barré and describes the clinical findings in a case of a child of 8½ years. He studied the changes in the C.S.F. and in the blood proteins. He discussed fully the differential diagnosis between polyradiculo-neuritis with a cell protein dissociation and diphtheritic polyneuritis due to other specific causes and poliomyelitis. Particular consideration was given to the origin of the increased albumin and globulin content of the C.S.F. and the correlation between this and alterations occurring in the histological structure of the nerve roots and the arachnoid. From the observed facts as to the raised blood protein especially the hyperglobulinæmia which runs parallel both to the albumin of the C.S.F. and the clinical course of the disease, the author is led to postulate, at any rate in this one case, a reaction of the reticulo endothelial cells, which he considers of special importance in the pathogenesis of the disease. (R. G. G.)

Chronic Dystrophy of Bone.—A case of localized osteoporosis of the skull is described in which the diagnosis was based upon the findings of local biopsy and confirmed by the subsequent history of the patient which was followed up for more than two years. The relation of this condition to various forms of bony dystrophy of the skull are considered and the ætiological factors discussed. The hypothesis put forward about the pathogenesis of localized osteoporosis of the skull confirms its individuality as a pathological entity and emphasizes the importance of exact diagnosis when considering prognosis. (R. G. G.)

Insulin and Cardiazol Therapy.—The author describes the results obtained by insulin and cardiazol in schizophrenia and schizoid syndromes and concludes that it is the antisymptomatic action which is of primary importance, and that in this field it represents a real advance in the treatment of mental disease. (R. G. G.)

Neurasthenia and Alterations in Midbrain and Spinal Cord.—Eight cases of this syndrome are described. The alterations in the midbrain and spinal cord were responsible for changes in the response of the pupils to light and in the deep reflexes. The history, clinical course, C.S.F. changes, and radiological changes in the skull bones, point to a degenerative rather than an inflammatory cause for this syndrome. It is correlated by the author with Adie's disease which has recently been considered to be degenerative. The syndrome now described differs from the latter in that the lesions responsible for the changes in the deep reflexes are in the pyramidal tracts rather than in the posterior columns. Moreover the infrequency of C..F. changes in Adie's disease is in agreement with the smaller extent of the organic lesions as compared with the syndrome here described. The midbrain lesions are common to both syndromes although they may be manifested clinically in different ways.
(R. G. G.)

Parenchymatous Lesions of Cerebellum in Carcinoma.—A woman of forty suffering from a malignant tumour of the uterus, developed a cerebellar symptom complex characterized by ataxia of the lower limbs, myoclonus and asynergia of the upper limbs, and nystagmoid clonic movement of the eyes. A diagnosis of secondaries in the cerebellum was made. A post mortem confirmed that the cerebellum was the seat of the lesion and histological examination showed a diffuse hyperplasia of the glial tissue of the brain especially of the cerebellum where there was a demyelinization in the region of the right dentate nucleus and to a lesser extent of the left, corresponding to the area of the greatest glial proliferation. In the cerebellar cortex there was some degree of atrophy of the Purkinje cells. The fundamental pathology of the gliosis and the relation of this to the demyelinizing lesions is discussed. The symptomatology is correlated with the anatomical losses in the capsule of the dentate nucleus and the exceptional character of the myoclonic movements which in some ways resemble myoclonus and in others a pedunculo striate tremor. (R. G. G.)

Epilepsy and Endocrines.—Ablation of one or both suprarenal cortices in dogs which were not predisposed to epileptic attacks following sensory stimulation and which had been shown to have a constitutional excess of cortical hormone was found to lead not only to a noteworthy

increase in the cortical excitability but also to an increased predisposition to epileptic attacks. In such animals the parenteral administration of an extract of whole suprarenal gland leads to diminution of the cortical excitability and to a disappearance of the predisposition to epileptic attacks following sensory stimulation. (R. G. G.)

SCHWEIZER ARCHIV FÜR NEUROLOGIE UND PSYCHIATRIE

Vol. 45. No. 1. 1940.

*Ausgewählte, kritisch besprochene Beispiele zum Eherecht der Geisteskranken. (Critical review of selected examples of eligibility for marriage of the mentally afflicted.) B. Dukor. 1.
*Die genetische Einheitlichkeit der klinisch unkomplizierten Schwachsinnsformen. (Hereditary uniformity and uncomplicated mental defect.) C. Brugger. 140.
*Gewerbliche Gifte und Nervensystem. (Hereditary poisons and the nervous system.) F. Flury. 146.
*Anormalenzählung in Appenzell a.Rh.vom Jahre 1937. II Teil. (Statistics of mental abnormality in Canton Appenzell-on-Rhine for the year 1937.) A. Koller. 159.
*Das Verhalten der Reflexe im Insulinkoma. (The behaviour of reflexes in insulin coma.) S. Lups and F. Kranz. 213.
*Rorschachbefunde bei chronisch Lungentuberkulösen und Herzkranken. (Test results by Rorschach's method in cases of chronic pulmonary tuberculosis and heart disease.) F. Singeisen. 230.
*Les Symptômes Cérébraux et Psychopathologiques dans les Intoxications Professionelles par des Substances Anorganiques. (Cerebral and psychopathological symptoms in industrial poisoning by inorganic substances.) H. Steck. 248.

Eligibility for Marriage of Mentally Afflicted.—250 cases which came before the courts between 1912 and 1940 are considered, of which about one-fifth are outlined. The histories are followed by critical discussions of the problems involved and the opinions of the experts. Questions discussed are : (1) right to marry ; (2) annulment of marriage ; (3) divorce. Conditions described include mental deficiency, insanity, senility, etc. (H. de P.)

Hereditary Uniformity of Uncomplicated Mental Defect.—Discussions of the findings of various investigations on hereditary forms of mental defect show that different grades of defect are found in the same family, and even in 5 out of 60 pairs of uniovular twins. It is suggested that there may be dominant as well as recessive forms of mental deficiency. The severest forms of idiocy are least influenced by hereditary and most by environmental factors. The incidence of mental defect in the families of persons on probation is noticeably large. (H. de P.)

Hereditary Poisons and Nervous System.—Poisons are divided into organic and inorganic, and their effects are general and specific. No poison affects only the C.N.S., though some cause predominantly nervous symptoms and signs. Chemically quite different substances can give rise to similar clinical pictures in the chronic stage. In the acute stage they are more differentiated. Their general effects are probably due to penetration of the cell with resulting interference with cell-function and metabolism. The poisons act as chemical traumata to the organism as a whole. Some form depôts in various organs so that their effect may persist after removal of the patient from the noxious agent. Specific effects of organic compounds and heavy metals used in industry are described and suggestions for prevention and treatment outlined. (H. de P.)

Mental Abnormality Statistics in Canton Appenzell.—A follow-up of children found to be mentally abnormal in the years 1907 and 1922. About 60 per cent. have turned out better and about 20 per cent. worse than was anticipated ; 20 per cent. have remained approximately stationary. These results show that special education has justified itself. Of those who approach normality the majority are married and able to support their families. Among their children the proportion of defectives is as yet uncertain, but appears to be rather high. Those members of the original groups who have deteriorated include a large proportion who have physical defects, e.g. deafness, as well as mental. Results show the desirability of preventing propagation of defectives and of alcoholism. (H. de P.)

Reflexes in Insulin Coma.—Tests are described for depth of coma for use in shock therapy. Those considered of most value are the corneal and Babinski reflexes. Blood-sugar level is not a reliable test, as depth of coma is not necessarily proportional to fall in blood-sugar. Tables are given showing experimental time sequence of reflex changes in relation to insulin injection and sugar feed. (H. de P.)

Rorschach's Test Results in Pulmonary T.B. and Heart Disease.—It has been noticed that psychical changes often accompany chronic physical illness. Investigations are described on 50 cases of pulmonary T.B. and 40 cases of severe heart and circulatory disorders by objective tests. These show fundamental differences between the two groups. Tuberculous patients are typically extraverted and unstable. Heart patients are typically introverted and characterized by depression and chronic anxiety. Both groups show unimpaired intelligence, and a tendency to exaggerated interest in physiological and

pathological processes. The question is discussed whether these characteristics are merely exaggerations of those existing before the onset of illness, or are results of disease processes. (H. de P.)

Cerebral and Psychopathological Symptoms in Industrial Poisoning.—Results of poisoning by mercury and lead are described in detail and by manganese and thallium more briefly. Severe cerebral symptoms are more common with lead than mercury. Differential diagnosis between metallic poisons, endogenous psychoses, and organic diseases of the nervous system is discussed. (H. de P.)

BOOK REVIEWS

THE HYPOTHALAMUS AND CENTRAL LEVELS OF AUTONOMIC FUNCTIONS

(Res. Publ. Ass. nerv. ment. Dis. (1939) 20. Williams and Wilkins, Baltimore. 1940. Pp. 980. $10.00.)

It is indeed difficult to give a critical review of a volume to which many authors have subscribed. There is no doubt, however, that the general level is extremely high.

Following a précis in which standardization of anatomical nomenclature is aimed at—an excellent proposition—eight chapters are given over to the anatomy of this region of the brain. An excellent review of the work indicative of the presence of secretory cells is to be found in Chapter IV, and this is followed by an equally informative one dealing with the connections of the primate thalamus. The work on the vascular bed of the hypothalamus is of considerable interest.

Chapters X to XXV are given over to the study of the physiology of the hypothalamus. All are of a high standard. There is much that is new in these chapters and all neurologists would be well advised to study them with care.

The remaining nine chapters are classified under the title " Clinical Symposium." Several of these chapters, however, deal essentially with the pathological changes found in this region of the central nervous system. The attention of readers is drawn to the chapters on disturbances of temperature regulation in man following lesions of the hypothalamus, and to the most interesting work of White, who records the results of stimulating this region of the brain, upon cardiac rate, blood pressure and state of consciousness.

The excellent printing, illustrations and complete bibliography make this volume of the greatest value to all neurologists. Nothing but the highest praise is to be given for this most valuable contribution to our knowledge of the hypothalamus and no library of a neurologist would be complete without it.

DISEASES OF THE NERVOUS SYSTEM

W. Russell Brain

(Oxford University Press, London. Second Edition, 1940. Pp. 950. 30*s*.)

This is a book which will be welcomed by the student, for in fairly compact form is to be found most of the important information regarding diseases of the nervous system. The specialist, however, may well wish to differ from the author's opinion as expressed in many places. The X-ray photographs are unsatisfactory and it is hoped that in the next edition better paper for their reproduction may be available. The index is very complete. This second edition is a worthy successor to the first.

PSYCHOBIOLOGY AND PSYCHIATRY

Wendell Muncie

(Henry Kimpton. 1939. Pp. 739. 40*s*.)

This is a text-book. Like all text-books it contains nothing that is new, but here the likeness ends, for every student of psychiatry should read it and add it to his shelves. It was written at the invitation of Dr. Adolf Meyer and gives an account of the conceptions, teaching, and working methods of the Henry Phipps Clinic.

It is divided into four parts, and it is a pity that, like Gaul, it was not content with three, for the fourth is a " historical survey in bibliography of the development of the concepts underlying the principal reaction sets " in tabloid form, too abbreviated to be of value to those who do not know the works quoted from, and irritating beyond measure to read.

Part I is devoted to the psychobiology and methods of study of the healthy individual. The statements made are supported by synopses of experimental work, physiological and psychological. In Part II, Dr. Muncie states the method of examining patients and, with the help of case reports and life charts, describes the various reaction types. The psychoses are more fully and more competently described than are the neuroses. Part III contains a comprehensive account, without too much detail, of treatment. The technique, dangers and limitations of the convulsant methods are assessed.

PSYCHOLOGY AND PSYCHOTHERAPY

William Brown

(Edward Arnold & Co., London. Fourth Edition, 1940. Pp. 260. 12*s*. 6*d*.)

This book by an eclectic psychologist contains in addition to an account of the Freudian dogma and the chief deviations from it, an interesting account of the author's experience in treating the psychoneuroses of war, of which he had considerable experience. The method which he advocates in early cases is light hypnosis and re-living of the emotional experiences which precipitated the appearance of symptoms. He claims that this method, combined in some cases with physiotherapy, was of great value in restoring the patients to duty. There is a stimulating chapter on the psychology of peace and war, and one on psychical research, a subject not usually dealt with in books of this type. The book is pleasant reading.

COMPENDIUM OF REGIONAL DIAGNOSIS IN LESIONS OF THE BRAIN AND SPINAL CORD

Robert Bing

(Translated by Webb Haymaker)

(Henry Kimpton, London. Eleventh Edition, 1940. Pp. 292. 25*s*.)

This book gives a useful account of the symptoms and signs which are to be expected in lesions at the various levels of the nervous system. It is copiously illustrated with diagrams which correlate the anatomy with the clinical syndromes. One wishes that the localization of lesions in the brain and spinal cord was as easy as the diagrams in the book indicate. The translation is good, and the fact that eleven editions have been needed in the thirty years since the book was first published testifies to its usefulness.

THE SEXUAL PERVERSIONS AND ABNORMALITIES

Clifford Allen

(Humphrey Milford, Oxford University Press, London. 1940. Pp. 193. 7*s.* 6*d.*)

In a small compact volume of just under two hundred pages Dr. Allen deals briefly but efficiently with those aspects of human sexual behaviour which are usually regarded as pathological and anti-social. The book is a pioneer work and is the first of its kind to be published in this country. Treatment of the subject is mainly from the psycho-analytical standpoint and the volume contains little of interest to the neurologist as such. The various chapters cover a wide field. The first three are chiefly biological in content. In the fourth a much needed attempt is made to arrive at a satisfactory classification of the various perversions discussed in subsequent chapters. The last chapter is stimulating and is probably the most interesting because it treats of sexual abnormality in relation to its social background. In the past perversion has received scant treatment from the medical profession in this country, but it may now prove to be a subject of profound importance in the near future. For example, an increasing high percentage of male and female homosexuals in a population that will soon decline rapidly presents a problem which is not only a question of medical treatment but one which embraces the position of homosexuals as non-producers of children in a society which will depend upon a high birth-rate as a final condition of survival. It would be impossible in such a small space to join issue with Dr. Allen on such questions or on the various points which arise as a result of the treatment of sexual abnormality from the psycho-analytical point of view. These questions, however, only concern the specialist, and the book can be warmly recommended to the senior medical student and to the general practitioner who wants a brief but lucid account of sexual perversion as he may encounter it.

A TEXT-BOOK OF PSYCHIATRY FOR STUDENTS AND PRACTITIONERS

D. K. Henderson and R. D. Gillespie

(Oxford University Press, London. 1940. Pp. 660. 20*s.*)

The authors of this excellent and well-established text-book have made changes and additions to keep it abreast of the times. The chapter on psychopathic states has been rewritten in accordance with the sound views put forward by the senior author in his Salmon Lectures. Insulin and cardiazol treatment receive due attention, and there are many other indications of revision. The least satisfactory feature of the book remains its bibliographic references ; often a fact is communicated on the authority of some writer whose name is given without any further hint as to where the original article is to be found. Thus on p. 515 the reader is told that " A. Gordon has recently described six cases " in which an obsessional disorder became overtly psychotic ; but is offered no further help towards tracing this paper, which was, in fact, published in the *American Journal of Psychiatry* in 1926. The selection of articles to which special attention is drawn is sometimes parochial.

The useful chapter on occupational therapy might well be expanded in the next edition, which is sure to be called for. The chapter on " Psychoses and Psychoneuroses of War " has lived to justify its retention.

MODERN TREATMENT IN GENERAL PRACTICE. YEARBOOK, 1940

Edited by Cecil P. G. Wakeley

(The Medical Press and Circular. 1940. Pp. 312. 12*s*. 6*d*.)

This book has attained the object, in giving an account of diagnosis and treatment in a number of important conditions with the minimum of words, which it claims. This minimum of words, however, has caused its value to be less than it might have been had a lesser number of subjects been dealt with and the space saved thereby been devoted to fuller descriptions of diagnostic procedure : *e.g.* in an article on backache, knowledge of the Smith-Petersen routine of back examination is assumed, and although the reference to the technique is given, practitioners may find difficulty in obtaining the account. Articles on treatment of burns and tetanus under war conditions are particularly acceptable at this time.

The book will prove of considerable value to the general practitioner, not merely in problems which he has to deal with alone but also in gaining an appreciation of modern hospital routine.

A MANUAL OF HISTOLOGIC TECHNIQUE

Oscar A. Turner

(Henry Kimpton, London. 1940. Pp. 73. 10*s*. 6*d*.)

This little manual is written for technicians and students working in a general pathological laboratory where formalin fixation of tissue is routine. The presentation is simple and well organized. By following the general plan of the book a rather complete histological survey of the central nervous system is possible. Many of the technical methods, particularly the metallic ones, have vagaries and uncertainties with optimum conditions of fixation. The author takes cognizance of this and has avoided extreme simplification by including brief accounts of methods from which the modifications necessary after formalin fixation have been derived. The well-chosen bibliography makes it possible for the serious worker to go to source material. There are several excellent and more complete manuals which have been published in the past few years than this one. Also older books on general histological technique in their revised editions include the newer advances in neurohistological technique. Turner's manual might be compared to the manuals of the various hospitals for use of their resident staffs. It is splendid for ready reference and points the way to other methods.